LITERATURE REVIEW

A systematic review on the WHO´s global priority pathogens (GPP) list reported in animals, products, and by-products in Colombia

Revisión sistemática de la lista global de patógenos prioritarios (GPP) de la OMS reportados en animales, productos y subproductos en Colombia

Revisão sistemática da lista global de patógenos prioritários (GPP) da OMS relatada em animais, produtos e subprodutos na Colômbia

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Abstract

Background: The World Health Organization (WHO) published in 2017 a global priority pathogens (GPP) list for research and development of effective antibiotics. It is a catalog of bacteria that should be prioritized in the fight against antibiotic resistance. **Objective:** To collect and assess the scientific evidence on bacteria listed as GPP in animal food products and by-products in Colombia, identifying knowledge gaps and providing evidence-based recommendations. **Materials and Methods:** This review was conducted following PRISMA guidelines. Only original articles published in peer-reviewed journals were considered. **Results:** Twenty-one articles published between 2001 and 2021 met the inclusion criteria. The geographical areas of study were in the provinces of Antioquia, Cundinamarca (including Bogotá district), Santander, and Tolima. The main bacteria reported from the WHO´s list were fluoroquinolone-resistant *Salmonella*, methicillin-resistant and vancomycin-intermediate and resistant *Staphylococcus aureus*, and carbapenem-resistant ESBL-producing Enterobacteriaceae. The sources were feces, facilities, equipment, feed, animal drinking water, bedding material, animal tissues, and carcasses from broiler, laying hen, cattle, and pig production systems. **Conclusion:** Our findings enhance the understanding of the current dynamics of bacterial resistance in Colombia. Nevertheless, several aspects need to be further researched, such as defining standardized methods for microbiological identification in veterinary medicine, as well as evaluating antibiotic susceptibility patterns of bacteria in accordance to what is done in humans, among other aspects.

Keywords: *animal; animal food product; antibiotics; antibiotic resistance; bacterial resistance; Colombia; drug-resistant bacteria; Enterobacteriaceae; pathogen resistance; resistant bacteria; Salmonella; Staphylococcus aureus; super-bacteria.*

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Resumen

Antecedentes: La Organización Mundial de la Salud (OMS) publicó en 2017 una lista global de patógenos prioritarios (GPP) para la investigación y desarrollo de antibióticos efectivos. Dicha lista consistente en un catálogo de bacterias a priorizar en la lucha contra la resistencia bacteriana. **Objetivo:** Recolectar y evaluar los hallazgos científicos en Colombia sobre bacterias catalogadas como GPP en animales y sus productos y subproductos, identificando vacíos en el conocimiento y brindando recomendaciones basadas en evidencia. **Materiales y métodos:** La revisión se llevó a cabo siguiendo las guías PRISMA. Solo se consideraron artículos originales publicados en revistas revisadas por pares. **Resultados:** Veintiún artículos publicados entre 2001 y 2021 cumplieron con los criterios de inclusión. Las áreas geográficas de estudio fueron los departamentos de Antioquia, Cundinamarca (incluyendo Bogotá D.C), Santander y Tolima. Las principales bacterias reportadas dentro de la lista de la OMS fueron *Salmonella* resistente a fluoroquinolonas, *Staphylococcus aureus* resistente a meticilina e intermedio y resistente a vancomicina, y Enterobacteriaceae productoras de BLEE resistentes a carbapenem. Las fuentes fueron heces, instalaciones, equipos, alimento concentrado, agua de bebida de los animales, material de cama, tejidos animales y canales de sistemas de producción de gallinas, pollo de engorde, bovinos y porcinos. **Conclusiones:** Nuestros resultados aportan al conocimiento del fenómeno de resistencia bacteriana y sus dinámicas en Colombia. Sin embargo, quedan varios aspectos por investigar, tales como los métodos estandarizados para la identificación microbiológica en medicina veterinaria, así como la evaluación de los patrones de susceptibilidad antibiótica de bacterias de acuerdo a como se hace en humanos, entre otros aspectos.

Palabras clave: *animal; antibióticos; bacterias resistentes; bacterias resistentes a los medicamentos; Colombia; enterobacterias; producto animal; resistencia a patógenos; resistencia antibiótica; resistencia bacteriana; Salmonella; Staphylococcus aureus; superbacterias.*

Resumo

Antecedentes: Em 2017, a Organização Mundial da Saúde (OMS) publicou a lista global de patógenos prioritários (GPP) para pesquisa e desenvolvimento de antibióticos eficazes; um catálogo de bactérias a serem priorizadas na luta global contra a resistência bacteriana aos antibióticos. **Objetivo:** Coletar e avaliar as evidências científicas sobre bactérias classificadas como GPP em animais e seus produtos e subprodutos na Colômbia, identificando lacunas de conhecimento e fornecendo recomendações com base nos resultados. **Materiais e métodos:** A revisão foi realizada de acordo com as diretrizes PRISMA. Apenas artigos originais publicados em periódicos revisados por pares foram considerados. **Resultados:** Vinte e um artigos, publicados entre 2001 e 2021, atenderam aos critérios de inclusão. As áreas geográficas de estudo foram os departamentos de Antioquia, Cundinamarca (incluindo Bogotá CD), Santander, e Tolima. As principais bactérias da lista da OMS relatadas foram *Salmonella* resistentes às fluoroquinolonas, *Staphylococcus aureus* resistentes à meticilina e intermediários e resistentes à vancomicina e Enterobacteriaceae produtoras de ESBL resistentes aos carbapenem. As fontes foram fezes, instalações, equipamentos, ração concentrada, água de bebida animal, cama, tecidos e carcaças, e referentes a frangos de corte e poedeiras, bovinos e suínos. **Conclusões:** Os resultados aqui obtidos permitem avanços importantes no conhecimento do fenômeno e sua dinâmica na Colômbia. No entanto, muito ainda precisa ser investigado no país, incluindo métodos padronizados de identificação microbiológica em medicina veterinária, bem como a avaliação de padrões de suscetibilidade a antibióticos em bactérias de acordo com o que é feito em humanos, entre outros aspectos.

Palavras-chave: *animal; antibióticos; bactérias resistentes; bactérias resistentes aos medicamentos; Colômbia; enterobactérias; produto animal; resistência a patógenos; resistência antibiótica; resistência bacteriana; Salmonella; Staphylococcus aureus; superbactérias.*

Introduction

Antibiotic resistance (AR) is one of the biggest threats to global public health, food safety, and country growth (WHO, 2020). Even though acquired resistance by microorganisms is a natural evolutionary phenomenon, it has been accelerated by widespread use and misuse of antibiotics in humans and animals, leading to selective pressure favoring bacteria capable of defeating antibiotics frequently used to treat common infections (Camou *et al.*, 2017).

The World Health Organization (WHO, 2017) published a global priority pathogens (GPP) list for the research and development of effective antibiotics. The list is a catalog of one family and 11 species of bacteria grouped according to AR. It aims to guide and align us in the global fight against resistant bacteria.

The Colombian National Health Institute (INS, by its name in Spanish) has implemented laboratory surveillance programs to identify circulating mechanisms of AR in the country. Since 2014, the Colombian Agricultural Institute (ICA, by its name in Spanish) has been monitoring AR for *Salmonella* spp., *Enterococcus* spp*.*, *Escherichia coli*, and *Staphylococcus* spp. recovered from eggs and milk. Additionally, the Colombian National Institute for Food and Drug Surveillance (INVIMA, by its name in Spanish) carries out laboratory-based monitoring of enteropathogens recovered from animal food products (WHONET, 2021). Furthermore, the Colombian Corporation for Agricultural Research (AGROSAVIA) and the Pan American Health Organization (PAHO) launched in 2010 a pilot for the Colombian Program for Integrated Surveillance of Antimicrobial Resistance (COIPARS) in the poultry chain, which included poultry farms, processing plants and supermarkets, involving the public and private sectors (Donado *et al.*, 2015).

Given that most bacteria included in the WHO´s list can also affect animal health, they could become major spreaders of resistance genes either through direct contact with humans or via the food chain. Therefore, it is vital to articulate and strengthen antimicrobial surveillance in different environments.

Although several studies on the topic have been published, the current AR scenario in Colombian animals and animal products is still unclear. Therefore, this review was aimed to collect information on bacteria listed by the WHO as GPPs in animals and their products in Colombia identifying knowledge gaps on the topic and providing evidence-based recommendations.

Materials and Methods

This systematic review (SR) was designed, performed, and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page *et al.*, 2020). An *a priori* protocol was carried out, including definition of the research question, literature search, inclusion and exclusion criteria, checklists for conducting relevance screening, characterization, methodological assessment, and data extraction on relevant primary research. No previous standardized SR have been published so far on the topic for this country.

Search strategy

Identification of relevant articles published in the scientific literature was guided by the following research question: What bacteria, listed by the WHO as GPP, have been reported in animals and their products and by-products in Colombia?

The search procedure was performed on January 31, 2023. The following search platforms were considered: OVID®/MEDLINE, PubMed®, SciELO Citation Index, and Redalyc. The research question was divided into components and the search terms were used to detect relevant citations in the platforms, as follows: [(bacteri* OR microorganism* OR pat$ogen* OR microb* OR aislamiento* OR aislado* OR isolat* OR cepa* OR strain*)] AND [(acinetobacter baumannii OR pseudomonas aeruginosa OR enterococcus faecium OR staphylococcus aureus OR helicobacter pylori OR campylobacter OR salmonel* OR neisseria gonorrhoeae OR streptococcus pneumoniae OR haemophilus influenzae OR shigella OR escherichia coli OR yersinia OR citrobacter OR enterobacter* OR klebsiella OR erwinia OR serratia OR hafnia OR edwardsiella OR proteus OR morganella)] AND [(antibio* OR antimicrobi* OR anti$infec* OR tratamiento* OR treatment*)] AND [(resist* OR sensi$i* OR multi$resist*)] AND [(animal* OR pet* OR mascota* OR abasto OR livestock OR canin* OR dog* OR perr* OR canid* OR bitch* OR feli* OR cat? OR gato? OR wild? OR silvestre* OR exotic? OR fauna OR caprin* OR goat? OR cabr* OR goatling? OR sheep OR ovej* OR lamb* OR cordero? OR caballo* OR horse* OR ye$ua* OR mare* OR potro* OR foal* OR bufal* OR porcine OR pig* OR cerd* OR pork? OR swine OR sow? OR lechon* OR bovi* OR cattle OR ganad* OR vaca* OR cow? OR toro? OR bull? OR heifer? OR novill* OR calf OR calves OR terner* OR water? OR agua*)] AND colombia*.

In addition, all 14 proceedings of the National and International Meetings of Researchers in the Livestock Sciences (ENICIP, by its name in Spanish) were searched. ENICIP is a biennial event that takes place in Medellin (Colombia) and is published since 1992 in the Revista Colombiana de Ciencias Pecuarias journal (https://revistas.udea.edu.co/index.php/rccp). This material was hand-searched for abstracts publishing primary studies. Finally, references on related subjects were hand-searched in Arenas and Melo (2018) to track primary publications.

Eligibility criteria

Inclusion criteria considered only articles published in peer-reviewed journals. Findings were not limited by year, country of publication, or language.

Systematic process for article selection

The first selection of citations was done according to the information contained only in the title. Two of the authors (LC, NC) completed the selection and a *kappa* coefficient was estimated. Exclusion criteria were: i) irrelevant topics (e.g., cancer, water treatment, *in vitro*, COVID, essential oils); ii) species other than the animals of interest or in the environment (e.g., human, mouse, rats, rabbit, soil, water treatment plant); iii) not the country (e.g., United States, United Kingdom, Brazil, Argentina, Ireland); iv) not an original article (e.g., review, book); v) other languages than English, Spanish or Portuguese (e.g., German, Russian). Duplicated articles were not considered. All citations selected by at least one of the two authors were considered eligible to continue in the process.

Eligible citations were screened by two authors (LC and LV) using the abstract. A *kappa* coefficient was estimated. The exclusion criteria were the same as for the title screening. Conflicts were resolved through consensus between authors and the third author (NC) was consulted when needed,

The full text of selected articles was reviewed by two authors (LC and NC) to identify and extract relevant information to answer the research question. A *kappa* coefficient was estimated. Articles were considered eligible using the same exclusion criteria described above. Conflicts were resolved through consensus between authors and the third author (LV) was consulted when needed.

The ENICIP proceedings and other abstracts identified during the primary search were revised by one of the authors (LV). In this regard, abstracts found able to answer the research question were identified and an email was sent to the corresponding author to inquire if the abstract was furtherly published in a peer-reviewed journal. The articles obtained from this previous stage were screened by two of the authors (LC and NC).

Finally, two authors (LC and LV) hand-searched the reference lists of relevant articles -identified by the full-text screening- looking for additional published primary articles (snowballing I). The same strategy was applied by two of the authors (LC and NC) for the same purpose to the reference lists of relevant articles identified by the snowballing I (snowballing II), as well as those detected in the references of the review by Arenas and Melo (2018). The work-database is available as Supplementary material.

Data extraction and descriptive statistics

After all available articles were compiled, data extraction was performed by two authors (LC and LV) independently. This extraction defined a final version by consensus. It considered bibliographic information (i.e., year, journal, country, language of publication, and author´s affiliations) and specific information to answer the research question (i.e., WHO´s GPP-related isolated bacteria, province of report, animal/environmental source, matrix, and AR-detection method, and inhibition halo, Minimal Inhibitory Concentration —MIC, resistance profile and genes, when applies).

Results

The combined results from the search databases yielded 1,959 eligible citations (after deduplication) potentially related to the subject of this review. The final number of articles fulfilling the eligibility criteria and hence included in the qualitative synthesis was 21. Figure 1 describes the review protocol and selection of relevant articles.

Twenty-one selected articles were published between 2001 and 2021 in 17 journals from eight countries. Sixteen were published in English and five in Spanish. Five of the relevant articles were coauthored by researchers affiliated to governmental agencies in Colombia (AGROSAVIA and ICA). Colombian universities (public and private) participated in 20 of the 21 articles. Foreign universities (public and private) and institutes participated in 9 of the 21 articles. Bibliometric information extracted from the relevant articles is available as Supplementary material.

The following proportions correspond to unique as well as combined results. The main geographical areas of study were the provinces of Antioquia (8/21; 38%), Cundinamarca (including Bogotá C.D; 7/21; 33%), and Santander plus Tolima (5/21; 23.8%, respectively). Sources consisted mainly of broilers and laying hens (10/21), cattle (7/21), pigs (4/21), feces (i.e., at the farm, in trucks and pens in the pre-farm), facilities, equipment, feed, animal drinking water, bedding material (3/21), tissues (e.g., heart, liver, gallbladder, intestine, pancreas, cecal tonsil, ovarian, oviduct), and carcass (i.e., 4/21).

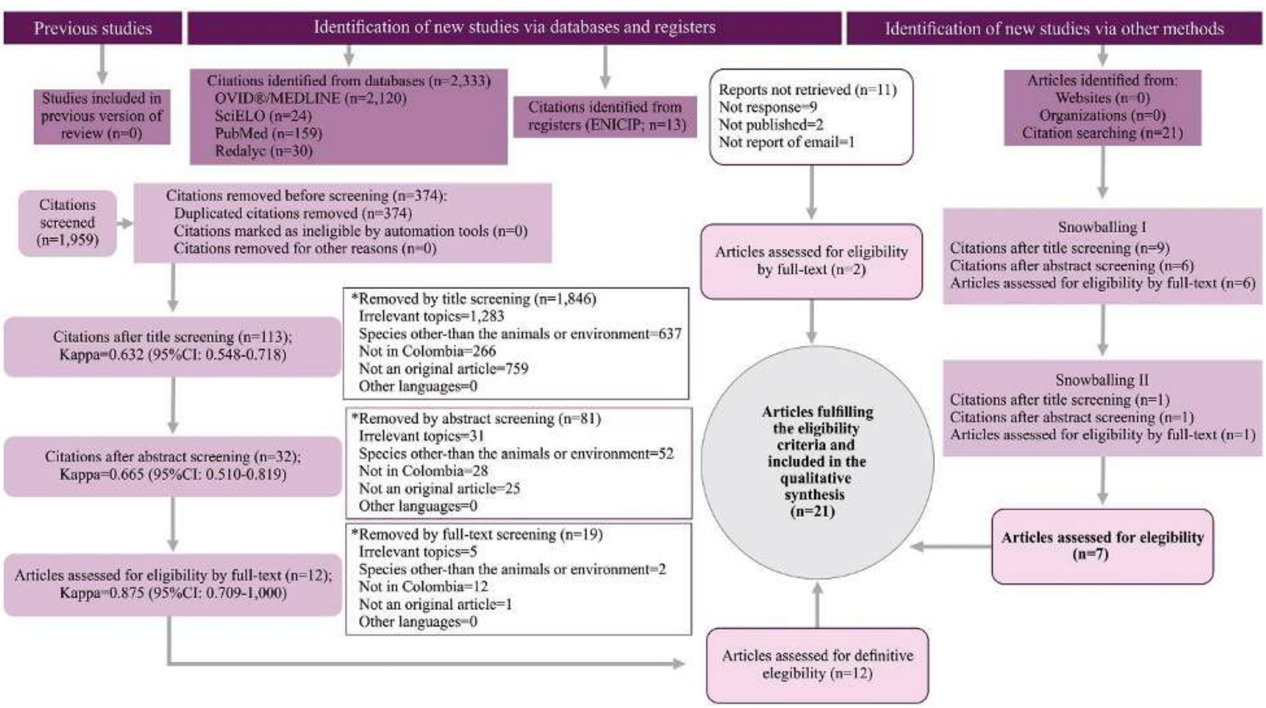

Figure 1. Flow-chart of relevant article selection (PRISMA, 2020) describing the progress of the citations through the systematic review.

The main bacteria from the WHO´s list reported by the relevant studies included in this review (considering combined results for one study) were fluoroquinolone-resistant *Salmonella* (12/21), methicillin-resistant and vancomycin-intermediate and resistant *S. aureus* (6/21), and carbapenem-resistant ESBL-producing Enterobacteriaceae (4/21). The AR-definition lab methods (considering combined results per study) included disk diffusion test (15/21), microdilution broth method (13/21), and PCR (9/21).

Table 1 presents findings extracted from the relevant articles. Figure 2 shows the geographical distribution of WHO GPPs by bacteria/family, animal species, and matrixes. Geographical distribution of isolates by province and bacterium is available under request to the corresponding author.

Discussion

Studies on AR in animals, their products and by-products in Colombia were reviewed for the first time herein using a well-defined systematic approach. This report aimed to present all the available data on bacteria listed in the GPP in the country by the WHO, identifying knowledge gaps and providing recommendations.

Several clarifications to our results should be made. The research question of this SR was related to animal, animal products, and animal by-products. However, information related to the isolation matrix was presented herein since it is in direct contact with the animals and, therefore, it represents a risk. Other articles on the same bacterial agents of interest (WHO´s) were not included since they lack the resistance profile considered in the research question. This is a qualitative report and, therefore, it cannot estimate the magnitude of the problem nor its behavior over time. Apparently, there are more research approaches in some of the provinces since the main cities of the country are located there and host the most important universities. Therefore, high frequency of reporting does not mean that the problem is more serious than in other parts of Colombia. In addition, some provinces can have a stronger surveillance system since they have greater potential in animal production and agriculture and, therefore, there could exist greater governmental interest.

Reports of strains of fluoroquinolone AR-*Salmonella* spp. have increased and spread worldwide (WHO, 2020) being recognized as a multi-resistant microbial species since the 90's (Guerra *et al.*, 2000). These strains are predominantly of zoonotic origin and develop resistance in the food-animal-host connection before transmission to humans through the food chain (Threlfall, 2002). In addition, *Salmonella* spp. is the main causal agent of bacterial diseases transmitted through food in the world (Brown *et al.*, 2021). According to WHO, it is a high category pathogen in terms of threat to human health (WHO, 2017). This agrees with the results obtained herein since *Salmonella* spp. was the most frequently reported bacterium. This confirms the importance of increasing research focused on improving public health globally and, of course, locally.

According to reports from 22 years of surveillance (1997-2018) by the Colombian INS, approximately 30% of human diarrheal outbreaks in Colombia are caused by this pathogen, and the primary source of infection is still unknown (INS, 2019). This link could be resolved based on the results of the present review, where animals, animal products, and by-products have been the source of isolation of fluoroquinolone AR-*Salmonella* spp.

Methicillin-resistant and vancomycin-intermediate and resistant *S. aureus* was second in frequency. This bacterium is an important cause of nosocomial illnesses worldwide, also related to substantial morbidity and mortality in humans at hospital and community-levels (Chen and Huang, 2014). Lately, the epidemiology of methicillin-resistant *S. aureus* (MRSA) has changed with the increasing occurrence of livestock-associated MRSA (LA-MRSA), which has been observed in farm animals (mainly pigs and cattle) and workers in close contact with MRSA-carrier animals (Chen and Wu, 2021; Molineri *et al.*, 2021).

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Recent reports indicate that MRSA isolates obtained from livestock and related workers are frequently indistinguishable, suggestive of cross-species transmission (Khanna *et al.*, 2008). Notably, clinical and virulence data indicate that this new LA-MRSA has potential for serious and fatal infections in humans (Lewis *et al.*, 2008; He *et al.*, 2018), hence the importance of identifying likely sources in animal production chains due to public-health risk that warrants close monitoring. A previous SR found 53 related studies were veterinarians and workers from livestock industries (swine, cattle, horse, poultry) and slaughterhouses presented significant decreasing risks, with an overall 9.80 OR (95% CI: 6.89-13.95) for livestock workers and veterinarians (Chen and Wu, 2021). Such findings led the authors to conclude that livestock-related workers, mainly swine farmers, are at significantly greater risk for LA-MRSA infection. These results strengthen the need for preventive practices to reduce LA-MRSA risk among people in close contact with livestock.

Regarding pets, MRSA transmission generally occurs through direct contact (e.g., contact with a wound, medical equipment, clothing) or contact with a symptomatic carrier (including animals) (Snyder *et al.*, 2008). Since staphylococcal bacteria can colonize human skin and nares, transmission can occur via the hands of a health-care provider (Cookson *et al.*, 1989). MRSA-positive isolates from cats —classified as healthcare-associated strains (HC-MRSA) in an 8-week follow-up were reported (Coughlan *et al.*, 2010). The study was conducted in a long-term care facility where family pets are allowed to visit convalescing patients or support animal-therapy programs. Although human MRSA infections occurred in the facility, it is unsure if pets served as an active source of infection to the humans in that study.

Bacteria from the Enterobacteriaceae family (different from *Salmonella* spp.) have an important impact in human and veterinary health (Farmer *et al.*, 2010). The family Enterobacteriaceae includes pathogens usually causing community-acquired infections as well as health care associated infections such as enterotoxemia and enterobacteremia, catheter-associated urinary tract infections, and located surgical infections (Janda and Abbott, 2021). Likewise, several of the major foodborne bacterial pathogens are members of this family (Bintsis, 2017) and, indeed, this is a dissemination pathway that has received more attention from the *One Health* approach (King, 2012). Since these pathogens are part of human and animal microbiota, it has been considered that animals could be reservoir of antimicrobial resistance genes that encode, for example, production of extended spectrum β-lactamases and carbapenemases (Castellanos *et al.*, 2017; Madec and Haenni, 2018).

One of the reports included herein assessed the resistance profile of isolates from clinical samples of diseased companion animals (Gómez *et al.*, 2020). It estimated that close contact and interactions with animals is a possible way for resistant bacteria acquisition, as reported worldwide (van den Bunt *et al.*, 2020; Roscetto *et al.*, 2021). Other six studies focused on the presence of enterobacteria as contaminant of foods of animal origin and their feasible entry to the food chain (Karczmarczyk *et al.*, 2010; Donado *et al.*, 2015; Castellanos *et al.*, 2017; Vásquez-Jaramillo *et al.*, 2017; Cortes *et al.*, 2017; Castellanos *et al.*, 2018). As reported in these studies, the presence of ESBL-producing enterobacteria has been informed from different food sources (Geser *et al.*, 2012; Tekiner and Özpınar, 2016; Madec *et al.*, 2017; Alegría *et al.*, 2020) in different stages of the food production chain (Ojer *et al.*, 2017; Musa *et al.*, 2020; Galler *et al.*, 2021). The latter underlines the necessity of good manufacturing practices, considering that some foods are consumed raw given their nature, ignorance, or culture (Madec and Haenni, 2018). The majority of enterobacterial isolates reported herein were sensitive to carbapenems, possibly because this group is still limited for use in humans but not for veterinary practice (Madec and Haenni, 2018; OIE, 2018).

Table 1. Question-related findings obtained from 21 relevant articles in the systematic review.

Reference	Isolated bacteria	Province of report	Animal/ environmental source	Matrix	AR detection method	Inhibition halo*	MIC**	Phenotypic resistance profile	AR genes
Ruíz *et al.* (2021)	*Staphylococcus aureus*	Antioquia	Cattle	Mastitis milk	Microdilution broth method	N/A	OXA ≤ 2.0; VAN ≤ 0.5 (NCCLS, 1999)	OXA(S); VAN(S)	N/R
Ruíz *et al.* (2006)	*Salmonella enterica* ser. Infantis, *Enteritidis*, Kedougou, Derby, Cerro, and Meleagridis	Antioquia	Laying hen	Facilities/ equipment/ feed/raw feed material/animal drinking water/ bed chip/tissues (heart, liver or gallbladder, intestine, pancreas, cecal tonsil, ovarian or oviduct tissues), feces	Microdilution broth method; Disk diffusion test	N/A	CIP ≤ 0.5 (NCCLS, 2000)	CIP(S)	N/R
Karczmarczyk *et al.* (2010)	*Salmonella enteritidis* ser. Uganda, Anatum, Braenderup, Newport, Carrau, Fresno, Javianam, Senftenberg, Adelaide, Bredeney, Derby, and Gaminara, *Salmonella enterica* subsp. *enterica* ser. Minnesota and Typhimurium	Atlántico; Sucre; Bolívar; Córdoba	Parrot/iguana/ hicotea turtle/ capybara/cattle/ pig/chicken	Sausages/raw and salted meat and viscera/ corn and egg mixture/potato/ cassava flour	Disk diffusion test	N/A	CIP ≤ 0.5 (CLSI, 2007)	CIP(S)	N/A
Donado *et al.* (2012)	*Salmonella enterica* ser. Paratyphi B variant Java, *Salmonella enterica* ser. Heidelberg	Santander; Cundinamarca	Broiler/ environment	Feces (at the farm)	Microdilution broth method; Disk diffusion test	ENR 32-40; NAL N/R	CIP ≤ 0.5; LVX ≤ 0.9 (CLSI, 2007)	CIP(I); LVX(I); ENR(R); NAL(R)	N/A

Table 1. *Continues...*

Reference	Isolated bacteria	Province of report	Animal/ environmental source	Matrix	AR detection method	Inhibition halo*	MIC**	Phenotypic resistance profile	AR genes
Cardona *et al.* (2013)	*Staphylococcus aureus*	Córdoba	Cattle	Navel swabs	Disk diffusion test	N/R	N/R	OXA(S); VAN(S)	N/R
Rodríguez *et al.* (2015)	*Salmonella enterica* ser. *Enteritidis* and *Shannon*	Tolima	Laying hen	Feces (at the farm)/feed and animal drinking water (at the farm)/egg	Disk diffusion test	N/R	CIP ≤ 2.0; LVX ≤ 0.5 (CLSI, 2007)	CIP(S); LVX(S)	N/R
Pulecio *et al.* (2015)	*Salmonella* spp.	Bogotá C.D.***	Pig	Feces (in trucks and pens in the pre-farm)/ mesenteric lymph nodes and cecal content (at the farm)	Disk diffusion test	N/R	CIP ≤ 2.0 (CLSI, 2008)	CIP (R)	N/R
Donado *et al.* (2015)	*Salmonella* spp., *Escherichia coli, Enterococcus faecium*	Bogotá C.D.***	Broiler	Raw meat	Microdilution broth method	N/A	VAN N/R; CIP N/R; LVX N/R; ENR N/R; NAL N/R; AMC N/R; CTX N/R; FEP N/R; CAZ N/R; CRO N/R; ETP N/R; IPM N/R; MEM N/R (CLSI, 2012)	*E. faecium*: VAN(S); *Salmonella* spp.: CIP (R); LVX(S); ENR(R); NAL(R); *E. coli*: AMC(S); CTX(S); FEP(S); CAZ(S); CRO(S); ETP(S); IPM(S); MEM(S)	N/A
López *et al.* (2017)	*Staphylococcus aureus*	Bolívar	Cattle/pig	Raw meat	Microdilution broth method; Disk diffusion test; PCR	N/R	N/R (CLSI, 2013)	N/A	mecA gene
Castellanos *et al.* (2017)	*Escherichia coli*	Cundinamarca; Santander; Sucre; Magdalena; Meta; Atlántico; Bolivar; Córdoba; Boyacá	Broiler	Feces (at the farm)/ cecal content and carcass rinsing (at the slaughterhouse)/ raw meat (at the slaughterhouse)	Microdilution broth method; PCR	N/A	CTX ≥ 4 (CLSI, 2013)	CTX(R)	blaCMY-2; blaSHV-12; blaSHV-5; blaCTX-M-2; blaCTX-M-15; blaCTX-M-8

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Table 1. *Continues...*

Reference	Isolated bacteria	Province of report	Animal/ environmental source	Matrix	AR detection method	Inhibition halo*	MIC**	Phenotypic resistance profile	AR genes
Vásquez-Jaramillo *et al.* (2017)	*Enterobacter cloacae, Serratia fonticola, Escherichia coli, Enterobacter cancerogenus*	Antioquia	Cattle	Raw milk	Microdilution broth method; Disk diffusion test; PCR	CFL 18; CXM 18; FOX 18; IMP 23	*E. coli*: SAM ≤ 9; FOX ≤ 4; CAZ ≤ 64; CRO ≤ 8; FEP ≤ 1; DOR ≤ 0.12; ETP ≤ 0.5; IPM ≤ 0.25; MEM ≤ 0.25; *E. cancerogenus*: SAM ≤ 16; FPX ≤ 4; CAZ ≤ 4; CRO ≤ 16; FEP ≤ 2; DOR ≤ 0.12; ETP ≤ 0.5; IPM ≤ 0.5; MEM ≤ 0.25; *E. cloacae*: SAM ≤ 4; FOX ≤ 4; CAZ ≤ 1; CRO ≤ 16; FEP ≤ 1; DOR ≤ 0.12; ETP ≤ 0.5; IPM ≤ 0.5; MEM ≤ 0.25; *S. fonicola*: SAM ≤ 32; FOX ≤ 16; CAZ ≤ 4; CRO ≤ 64; FEP ≤ 4; DOR ≤ 0.12; ETP ≤ 0.5; IPM ≤ 0.25; MEM ≤ 0.25 (CLSI, 2014)	*E. coli*: CFL(R); CXM(R); CAZ(R); CRO(R); FEP (R); FOX(S); IMP(S); SAM(S); DOR(S); ETP(S); MEM(S); *E. cancerogenus*: CFL(R); CXM(R); CRO(R); FOX(S); IMP(S); SAM (I); CAZ (S); FEP(S); DOR(S); ETP(S); IPM(S); MEM(S); *E. cloacae*: CFL(R); CXM(R); SAM(R); FOX(R); CRO(R); IMP(S); CAZ(S); FEP(S); DOR(S); ETP(S); IPM(S); MEM(S); *S. fonicola*: CFL(R); CXM(R); SAM(R); FOX(R); IMP(S); CAZ(S); CRO(R); FEP(S); DOR(S); ETP(S); IPM(S); MEM(S)	(bla gene) CTX-M; CTX-M-1; CTX-M 96/ CTX-M-12a
Cortes *et al.* (2017)	*Salmonella* spp.	Tolima	Broiler	Raw meat	Microdilution broth method; Disk diffusion test; PCR	N/R	CIP N/R; ENR N/R (CLSI, 2015)	CIP(R); ENR(R)	N/R

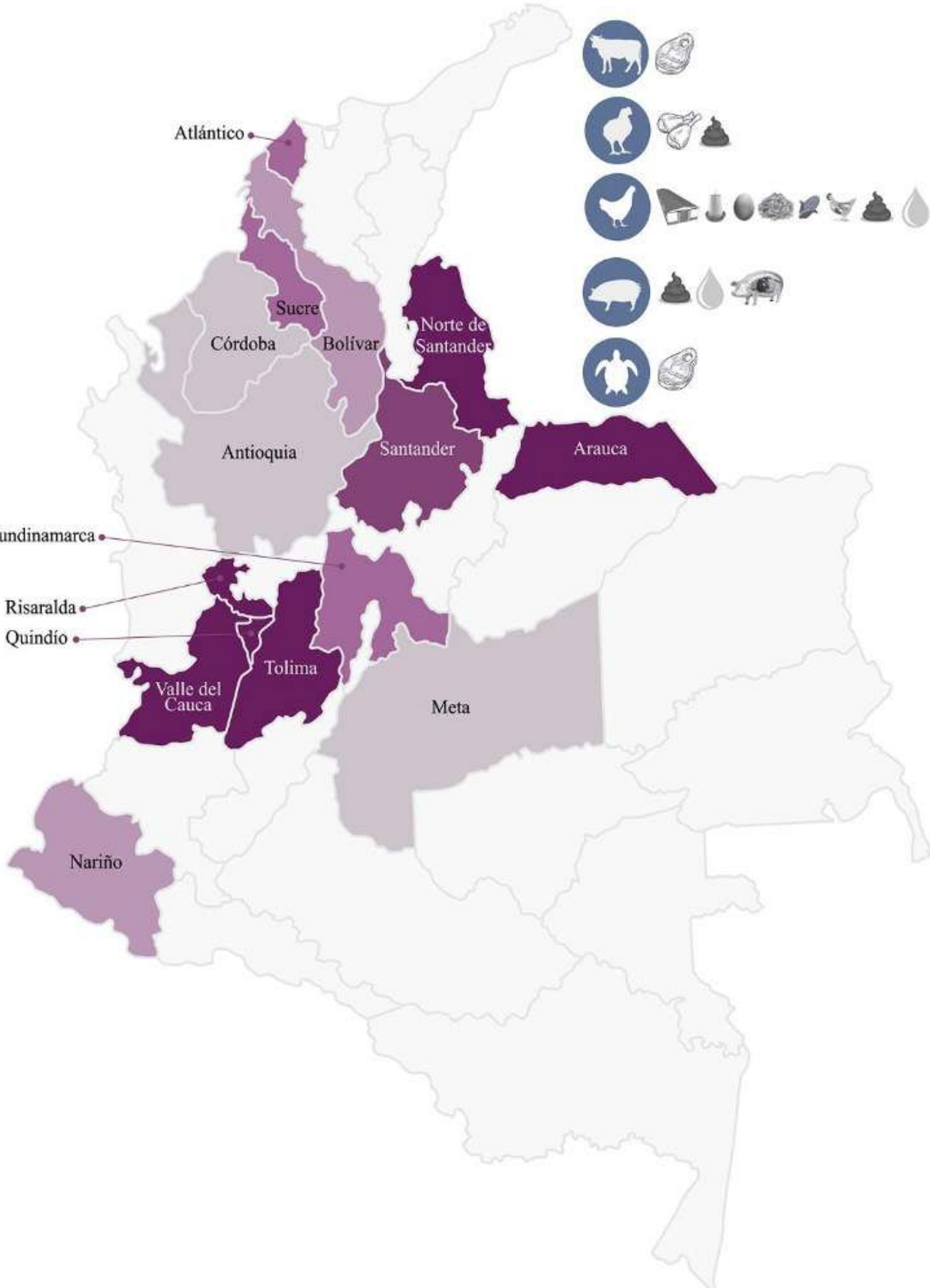
Table 1. *Continues...*

Reference	Isolated bacteria	Province of report	Animal/ environmental source	Matrix	AR detection method	Inhibition halo*	MIC**	Phenotypic resistance profile	AR genes
Castellanos *et al.* (2018)	*Salmonella enterica* ser. Heidelberg, Paratyphi B variante Java, *Enteritidis*, Kentucky, and Albany	Santander; Cundinamarca; Bogotá C.D.***; Sucre; Bolivar; Antioquia; Valle del Cauca; Nariño; Atlántico; Norte de Santander; Arauca; Tolima; Risaralda	Broiler	Feces (at the farm)/ carcass (at the slaughterhouse)	PCR	N/A	N/A	N/A	blaCTX-M-2 group; blaSHV family blaCMY-2-like; blaCTX-M-2 group; blaCMY-2-likeblaSHV family
Giraldo *et al.* (2019)	*Salmonella* spp.	Antioquia; Valle del Cauca; Eje Cafetero****; Cundinamarca; Meta	Pig/ environment	Feces (at the farm)/runoff water/animal drinking water	Microdilution broth method	N/A	CIP ≤ 2.0 (CLSI, 2007)	CIP(S)	N/A
Castro-Vargas *et al.* (2019)	*Salmonella enterica* ser. Heidelberg	Santander	Broiler	Feces (at the farm)	Microdilution broth method; Disk diffusion test; PCR	ENR 5	NAL ≤ 30; CIP ≤ 5; LVX ≤ 5 (CLSI, 2017)	CIP(R); LVX(R); ENR(S)	N/A
Fandiño and Verjan (2019)	*Salmonella enterica* ser. *Enteritidis*, Typhymurium, Newport, Grupensis, Uganda, and Braenderup	Tolima	Laying hen	Crushed eggshell/ eggshell surface wash	Microdilution broth method; Disk diffusion test; PCR	N/R	CIP N/R; LVX N/R; ENR N/R; NOR N/R (CLSI, 2014)	CIP(S); LVX(S); ENR(S); NOR(S)	N/R
Jiménez *et al.* (2020)	*Staphylococcus aureus*	Cundinamarca; Nariño; Meta; Cesar	Cattle	Raw milk	Disk diffusion test; PCR	N/R	OXA N/R (CLSI, 2019)	OXA(S)	mecA

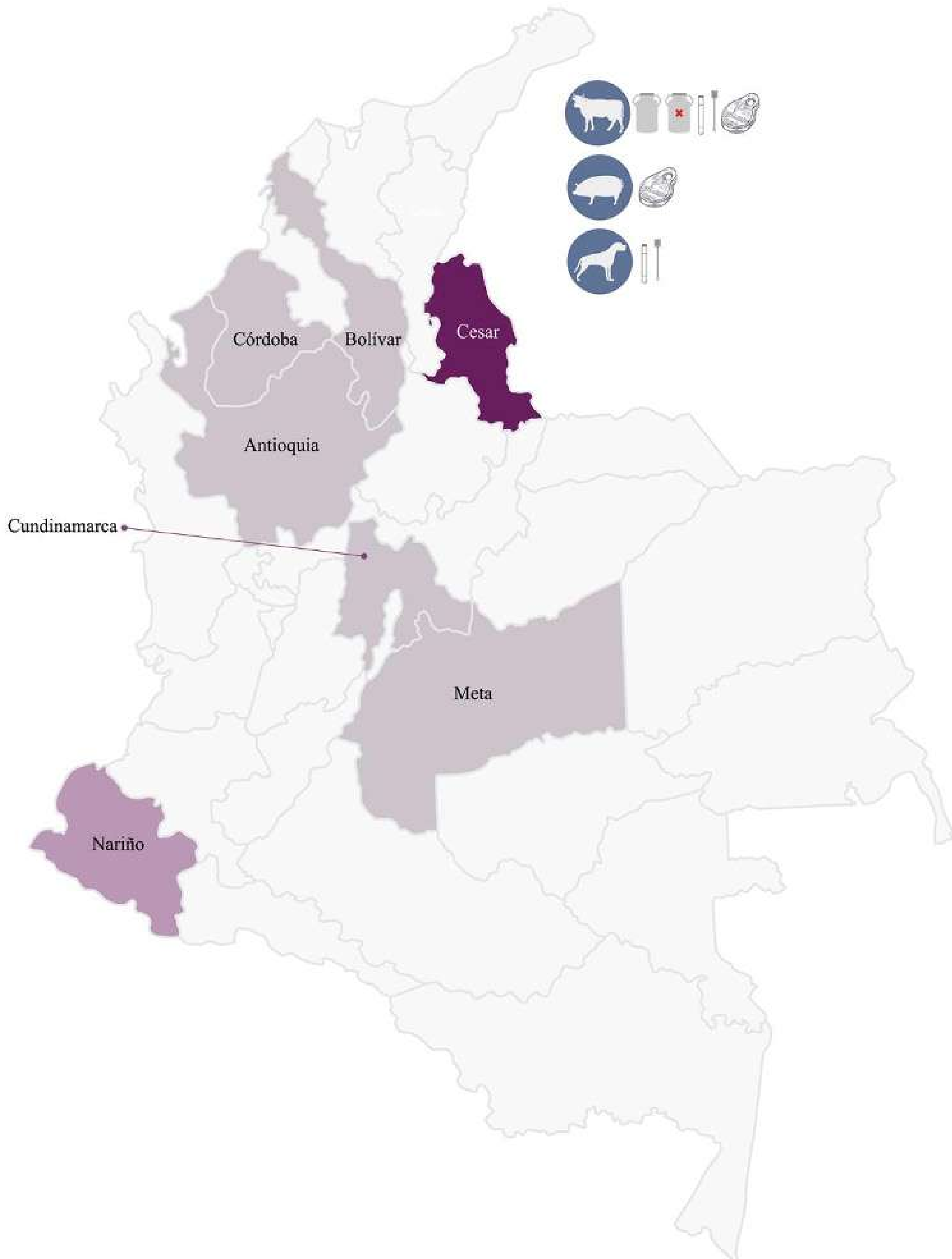
Table 1. *Continues...*

Reference	Isolated bacteria	Province of report	Animal/ environmental source	Matrix	AR detection method	Inhibition halo*	MIC**	Phenotypic resistance profile	AR genes
Gómez *et al.* (2020)	*Enterococcus* spp., *Escherichia coli*	Antioquia	Dog/cat	Urine/ears, active skin lesions, nasal cavity, and eyes swabs	Disk diffusion test	N/R	SAM N/R (CLSI, 2018)	SAM(S)	N/A
Torres *et al.* (2020)	*Staphylococcus aureus*	Antioquia	Cattle	Raw milk	Microdilution broth method	N/A	N/R	MET(S)	N/A
González *et al.* (2020)	*Staphylococcus aureus*	Antioquia	Dog	Active skin lesions swabs	Disk diffusion test; PCR	N/R	N/A	N/A	mecA
Herrera *et al.* (2021)	*Salmonella enterica* ser. Heidelberg, Paratyphi B, Newport, *Enteritidis*, Braenderup, Uganda, Typhimurium, and Grupensis	Tolima; Santander	Broiler	N/R	Microdilution broth method; Disk diffusion test	N/R	CIP ≤ 5; LVX ≤ 5; ENR N/R (CLSI, 2017)	CIP(R); LVX(R); ENR(R)	qnrB; aac (6')-Ib

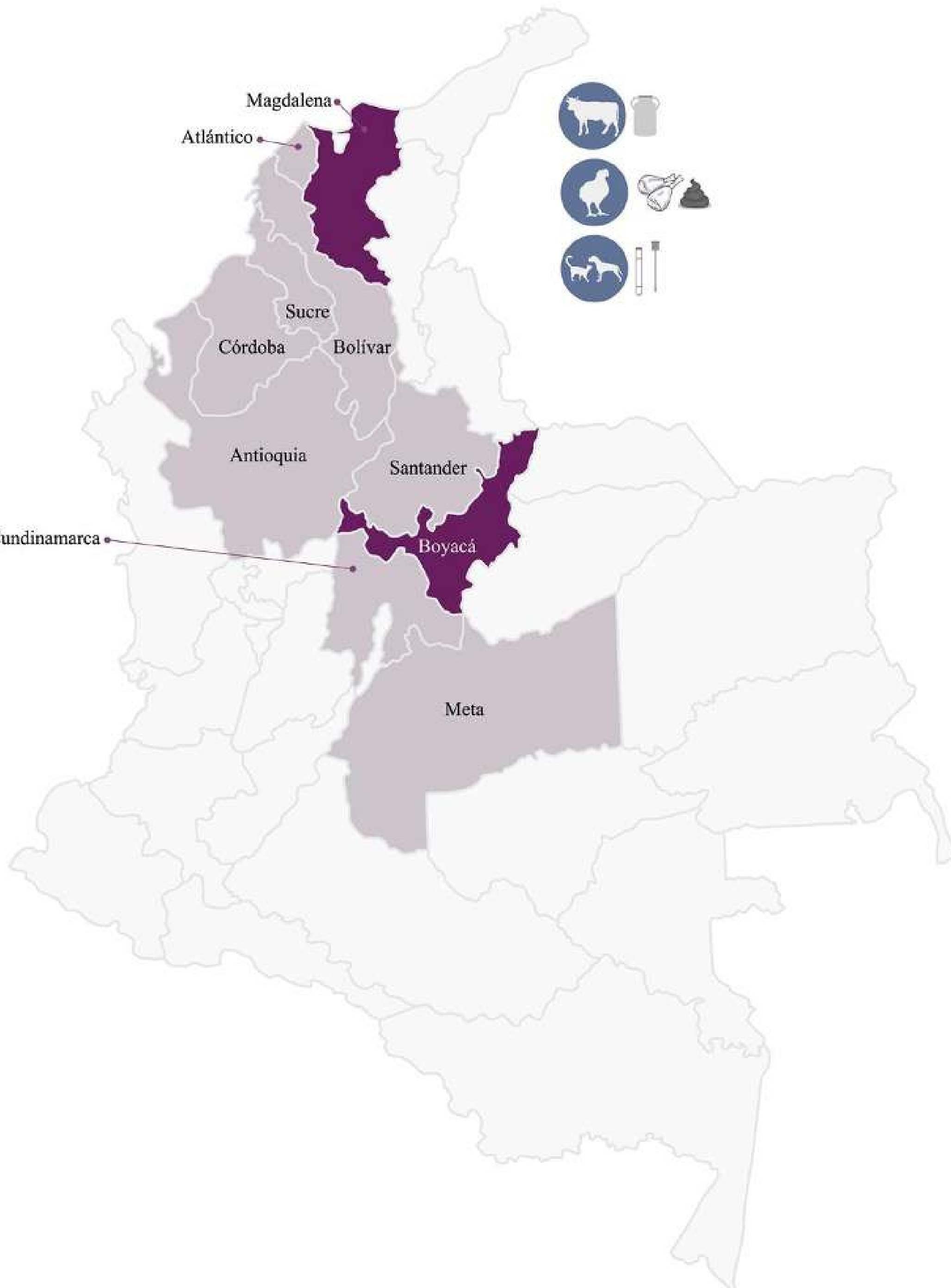
*Minimum Inhibitory Concentration for a *resistant* definition —in µL/mL or mg/L (reference guidelines); **For a *Sensitive* definition —in mm; ***Located in Cundinamarca province. ****Located between the provinces of Caldas, Risaralda, and Quindío. AR: Antimicrobial resistance; N/A: Not applicable; N/R: Not reported; MIC: Minimal inhibitory concentration; NCCLS: National committee for clinical laboratory standards; CLSI: Clinical and laboratory standards institute; (S): Sensitive; (I): Intermediate; (R): Resistant; OXA: Oxacillin; VAN: Vancomycin; CIP: Ciprofloxacin; ENR: Enrofloxacin; NAL: Nalidixic acid; LVX: Levofloxacin; AMC: Amoxicillin–clavulanic acid; CTX: Cefotaxime; FEP: Cefepime; CAZ: Ceftazidime; CRO: Ceftriaxone; ETP: Ertapenem; IPM: Imipenem; MEM: Meropenem; FOX: Cefoxitin; DOR: Doripenem; SAM: Ampicillin-sulbactam; NOR: Norfloxacin; MET: Methicillin; CFL: Cephalexin; CXM: Cefuroxime.


Atlántico
Sucre
Córdoba
Bolívar
Norte de Santander
Antioquia
Santander
Arauca
Cundinamarca
Risaralda
Quindío
Tolima
Valle del Cauca
Meta
Nariño

A


Córdoba
Bolívar
Cesar
Antioquia
Cundinamarca
Meta
Nariño

B



C

Figure 2. Geographical distribution of World Health Organization Global Priority Pathogens, by bacteria/family, animal and isolation matrix found in the studies conducted in Colombia (2001-2021). A: Fluoroquinolone-resistant *Salmonella*; B: Methicillin-resistant and vancomycin-intermediate resistant *Staphylococcus aureus*; C: Carbapenem-resistant ESBL-producing Enterobacteriaceae. The color scale of provinces corresponds to reporting frequency, with the darkest color representing the highest frequency.

According to the Colombian National Observatory of Health (ONS, by its name in Spanish; personal communication) AR to fluoroquinolones in humans during the last decade (2011-2021) (ciprofloxacin) was 0-2.5% in typhoidal *Salmonella*-related clinical cases and 0% in nontyphoidal *Salmonella* cases. The median of methicillin-resistant *S. aureus* was reported in 41.6% of infectious events and 8.7% in carriers; it was between 2.4 and 6.9% for *Klebsiella pneumoniae* to carbapenems (being higher for ertapenem with 6.9% resistance); and between 0.2 and 0.6% for *E. coli* to carbapenems (being higher for doripenem, with a median of 0.6%). This scenario constitutes a potential break in the 'species barrier', and the relevance that the findings of this review may have in decision-making at the country level.

The final number of articles included in the present SR is not minor, but it does represent a significant dilution over the last two decades. This could be due to budget restrictions, insufficient collaborative research within the region and among regions, lack of knowledge of the phenomena, and low research awareness.

Considering the data currently available, systematically reviewing the literature on this subject is difficult since there is substantial variability in study designs and research approaches. Consequently, information should be considered with caution since the outcome (i.e., bacteria listed by the WHO as GPP reported in animals and their products and by-products in Colombia) may vary from case to case.

Due to limitations in AR-related research and reporting at the country level, publication standards among articles were not considered since variability of the methods and reporting of results make a deeper analysis difficult. In addition, study designs are generally non-probabilistic, mainly from incidental cultures or strains, which compromises inferences from the results. On the other hand, there are economic constraints that limit the use of certain tools —such as reference guides for MIC interpretation. This compels researchers to use freely accessible but outdated guides as the basis for interpreting their results, compromising the scientific impact of some approaches. Even more critical is the absence of veterinary guidelines for the interpretation of results (e.g., MIC), since the available data correspond to those derived from plasma pharmacokinetic studies in humans. Likewise, this information is extrapolated to domestic animals for dosing antibacterial drugs in veterinary medicine. In addition, the previous appreciations correspond to only one facet of the problem since the AR-relationship between animals and humans has not yet been generalized at a country-level, being evaluated as two independent situations in most reports, hampering deeper analysis.

Despite the evidence found in the present SR, there is a need to analyze the food chain at a higher level and detail, identifying, when possible, the origin of infections. There is also a need to expand research to pets since they live in close contact with humans. Additionally, reports continue to focus on the regions of greatest socio-economic development in the country, which could differ from the reality of Colombian AR since reports from rural and poorer areas are limited.

The trend of AR is an increasing national problem given the absence of regulations or treatment guidelines for administration of medicines to animals, including antibiotics (e.g., a prescription is not required to buy antibiotics for animals). According to a survey by Gómez *et al.* (2021), there is a need for prudent use of antimicrobials in every clinical condition in pets in Colombia, including the use of diagnostic tests and selection of proper antimicrobial agents used in empirical treatments.

Regarding the strengths of AR-related research and reporting at the country-level, there is an increasing number of articles on AR in animals, their products, and by-products in Colombia reflecting a growing interest in the phenomenon and its impacts. It should be mentioned that most relevant articles in the present review were published in English -probably due to the need to attain greater visibility in the scientific community.

This SR has strengths and limitations. Regarding strengths, a clearly stated and delimited question-based protocol was used, and the eligibility of relevant studies was based on pre-established and precise inclusion/exclusion criteria. We performed a detailed literature search from several databases, including general-purpose, journals, proceedings, and books from 1910 to the present, with no geographic limitations. Two of the authors followed independent selection principles and results from each searching step were always consensual, reporting agreement measures along the process. Lastly, data extracted from relevant studies were clearly defined, and a matrix of findings was constructed, filled, and revised by all the authors. As for limitations, grey literature (papers, reports, technical notes, unpublished theses, and dissertations, or governmental or academic documents indexed by commercial publishers) was not fully considered since many of these documents are difficult to obtain. We tried to control this by the snowballing processes, leading to a maximum yield of relevant articles.

The research question established for this SR was answered. Nevertheless, much remains to be explored. The lack of resistance data in most of the country and the limited number of studies for some pathogens make it difficult to estimate the magnitude of the problem in veterinary medicine as well as in public health. There are significant information and knowledge gaps in livestock and farm animals such as sheep, goats, fish, rabbits, as well as in companion animals such as horses, dogs, cats, and non-conventional pets. There is also need for standardized methods for microbiological identification in veterinary medicine and evaluation of antibiotic susceptibility patterns of bacteria in accordance with what is done in humans (e.g., use of automated methods to speed up results and facilitate the analysis, instead of using disk diffusion; a cheaper but old, time consuming, and less accurate method). Finally, we consider important to report the values for sensitivity and resistance to carbapenems, at least in research-related reports. In addition, probabilistic studies are needed that allow to monitor the epidemiology of AR in both animals and humans during the same period, comparing findings in a precise way for a complete picture of the phenomenon.

Declarations

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Conflicts of interest

The authors declare they have no conflicts of interest regarding the work presented in this report.

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Author contributions

All authors contributed to the conception and design of the study. LC and NC proposed the research objective. The literature search and data analysis, as well as the critical revision of the manuscript was performed by all the authors. The first draft of the manuscript was written by LC and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Use of artificial intelligence (AI)

No AI or AI-assisted technologies were used during the preparation of this work.

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