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Letter to the editor

Bibliometric trends of scientific publications on antimicrobial resistance in *Escherichia coli* in Peru from 2009-2019

Tendencias bibliométricas de las publicaciones sobre resistencia a antimicrobianos en *Escherichia coli* en Perú de 2009-2019

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Mr Editor:

Antibiotics and microorganisms have coexisted for millions of years[1]. A series of microorganisms produce antimicrobials which contribute to their biological success. These microorganisms developed a series of pathways to avoid self-killing, which may be considered as proto-mechanisms of antibiotic resistance. Similarly, other microorganisms developed specific adaptations to minimize the effect of these substances, allowing their survival while in the vicinity of antibiotic-producers. Nevertheless, prior to the introduction of antibacterial agents in therapeutic in the 20th century, the presence of antibacterial agents in the different environments was extremely low, with these low levels of antibiotic production having an insignificant impact, limited to the surroundings of producers, and only relevant in very specific circumstances[2]. The introduction of either natural or nature-derived antibacterial substances or molecules of full-synthetic origin (hereafter collectively named "antimicrobial agents") into clinical practice in the first half of the 20th century and the subsequent exponential uncontrolled use in humans, animals and agriculture unbalanced the situation[1,3], leading to the selection of antimicrobial-resistant microorganisms and favoring the spread of mobile structures carrying antimicrobial-resistant determinants; with these microorganisms and structures expanding to different environments, including those with a high and clear anthropic pressure[4], as well as previously unspoilt areas[5].

At present, highly worrying scenario is occurred, with antimicrobial-resistant microorganisms being a silent pandemic affecting all countries irrespective of their income level and causing increasing mortality worldwide[6]. Furthermore, pan-resistant pathogenic microorganisms are increasingly being recovered, alerting about the risk of being unarmed against potentially lethal infections[6].

This situation has resulted in an escalating presence of antimicrobial resistance and its consequences in scientific publications. Thus, while scarce and testimonial during the first years after the introduction of antibiotics into clinical practice, from the second third of the 20th century onwards a

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CONFLICTS OF INTEREST
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fast grown of reports of antimicrobial-resistant pathogens may be observed in scientific literature. Thus, a sought in PubMed (https://pubmed.ncbi.nlm.nih.gov/) using the terms "(antibiotic resistance) OR (antimicrobial resistance)" showed the presence of 17 documents in 1945, 1,832 in 1980, 24974 in 2021 and16,868 on September 12, 2022.

Nevertheless, the publication scenario is unequal, with extensive literature related to high-income countries and limited data regarding most low- and middle-income countries. Furthermore, this inequity is most noticeable regarding studies beyond human health.

Peru is a middle-income country, in which over-the-counter access to antimicrobial agents is common[7]. This scenario, combined with sociocultural background, inequities and difficulties to access health facilities in different regions of the country, strongly contribute to the development and under-reporting of antimicrobial-resistant microorganisms.

Escherichia coli is classically the most studied microorganism. Its cosmopolitan distribution results in the possibility of its being described as a focus of human, animal, plant or environmental studies developed in any part of the globe. Furthermore, while several *E. coli* isolates display virulence properties and are isolated from almost all biological sources as a cause of human or animal infections[8-12], others are stable commensal members of different microbiotas[10,13]. Thus, this microorganism is a good model to study antibiotic resistance and to determine the "antibiotic exposure" of different sources and environments.

The aim of the present study was to analyze the bibliometric characteristics of publications focused on the levels of antimicrobial resistance of non-human disease-producing E. coli isolated in Peru during the period from 2009-2019.

A search was conducted on PubMed using the terms ((*Escherichia coli*) AND Peru) AND antibiotic resistance), in addition to a search in Google Scholar and local repositories. Only studies in Spanish or English with antimicrobial resistance data (i.e.: number or percentage of isolates in which antimicrobial resistance was established by disk diffusion and/or minimal inhibitory concentration) of E. coli not isolated as a cause of human infection were taken into account. When more than one article referred to the same bacterial collection, date of the first article published was considered to establish the delay in publication after sampling. When a thesis work was also present as an article, either PubMed (PM) or not-PubMed (NPM) included, only the published article was considered.

Overall, 67 studies were recovered from the different sources analyzed, 32 of which were excluded after visual inspection due to a lack of adherence to inclusion criteria.

The 35 studies selected referred to 30 different bacterial samplings, with two samplings reported in 5 and 2 manuscripts respectively. Among the manuscripts selected, 16 were indexed in PM, while 19 were from other sources, including 11 NPM indexed articles and 8 thesis, with the latter including 1 Doctoral, 2 Master and 5 Grade studies (Tables 1).

Human samples were the most commonly studied, being described in 11 (31.4%) studies, followed by those of livestock and environmental origin in 10 (28.6%) and 8 (22.8%) studies, respectively. Meanwhile pets, wild animal and food samples were present in 14.2%, 11.4% and 8.6%, respectively (Table 1). Analysis by thematic subtype also showed that reports including *E. coli* from human sources were all indexed in PubMed, while this finding was present in only a percentage of studies focused on E. coli from other sources, suggesting the perception of higher relevance because of the type of samples (Table 1).

All articles indexed in the Web of Science (WoS) were also indexed in SCOPUS. Thus, 24/27 (88.9%) articles were published in journals indexed in SCOPUS, with 13 (48.1% of total articles) also being indexed in WoS. Of these, 10 were indexed in Q1, 2 in Q2, 5 in Q3 and 7 in Q4 in at least one of the databases (Table 1).

Overall, 15/27 (55.6%) articles were authored by international teams including both Peruvian and foreign authors. Regarding the authorship of articles published in Peruvian journals, 9 out of 12 were signed by Peruvian authors only, while the remaining 3 were signed by mixed teams (Table 1). The journals with the highest number of publications were the Revista de Investigaciones Veterinarias de Peru, with 5 articles, and the American Journal of Tropical Medicine and Hygiene and the Revista Peruana de Medicina Experimental and Salud Publica with 3 articles each (Table 1). The mean number of articles related to the study subject published each year during the period analyzed was 2.5 articles, with a peak of 6 in 2019, demonstrating a low index of publications. The number of publications tends to increase in the last years. This increase in the last years of the series may be either a conjunctural fact or reflect an increase in reporting in this field.

The high proportion of unpublished (only reported in thesis format) studies is of note, accounting for 8 studies representing 21.6% of all studies included in the analysis according to the criteria established (Table 1). This finding magnifies the possible presence of undetected studies in thesis format in non-searched university on-line repositories or bibliotheca.

When sampling time was recorded, the time between sampling and data publication, either in article or thesis format, ranged from 0 to 18 years, with a median time of 3 years and mean time of 3.7 years. Of note, one environmental study described data from samples collected at least 18 years previously (Table 2). The mean time between sampling and publication was 3.2 years, excluding the latter study.This median time between sampling and publication was 4 years if only PubMed articles were considered, decreasing to 3 years when considering non-PubMed articles. When the time elapsed was analyzed by themes, the studies reporting E. coli from pets or environmental sources were those reported earlier, being published a median of 2 years after sampling, while those from alimentary sources were reported a median of 4.5 years after sampling, respectively (Table 2).

Table 1. Sources and indexing of articles published in the period 2009-2019.

Journal	Year	Source	Authors	Journals PJ	Journals PM	Quartile SCOPUS	Quartile WoS	DOI / WEBPAGE
Int J Antimicrob Agents	2009	H	IRT	N	Y	NF	Q2	10.1016/j.ijantimicag.2008.07.029
Antimicrob Agents Chemother	2009	H	IRT	N	Y	NF	Q1	10.1128/AAC.01722-08
Am J Trop Med Hyg	2009	H	IRT	N	Y	NF	Q1	10.4269/ajtmh.2009.81.296
Am J Trop Med Hyg	2010	F, H, L, Pt	IRT	N	Y	NF	Q1	10.4269/ajtmh.2010.09-0143.
J Antimicrob Chemother	2011	H	IRT	N	Y	Q1	Q1	10.1093/jac/dkr026
Rev Esp. Quimioterap	2012	E	P	N	Y	Q3	Q4	https://seq.es/wp-content/uploads/2012/06/seq.es_seq_0214-3429_25_2_rivera.pdf
Int J Antimicrob Agents	2012	H	IRT	N	Y	Q1	Q1	10.1016/j.ijantimicag.2012.07.021
Rev Inv Vet Peru	2012	L	P	Y	N	Q4	---	http://www.scielo.org.pe/pdf/rivep/v23n3/a04v23n3.pdf
Trans R Soc Trop Med Hyg	2013	H	IRT	N	Y	Q1	Q2	10.1093/trstmh/trt059
Trans R Soc Trop Med Hyg	2014	H	IRT	N	Y	Q1	Q2	10.1093/trstmh/trt106
Rev Inv Vet Peru	2014	Pt	P	Y	N	Q4	---	http://www.scielo.org.pe/pdf/rivep/v25n1/a09v25n1.pdf
Rev Peru Med Exp Salud Publica	2015	H	P	Y	Y	Q3	---	http://www.scielo.org.pe/pdf/rins/v32n4/a18v32n4.pdf
Salud Tecnol Vet	2015	L	IRT	Y	N	---	---	10.20453/stv.v3i1.2823
Rev Inv Vet Peru	2016	L	P	Y	N	Q4	---	10.15381/rivep.v27i2.11651
Am J Infect Control	2016	E	P	N	Y	Q1	Q2	10.1016/j.ajic.2016.02.020
Rev Latinoam Recurs Nat	2016	WA	P	N	N	---	---	https://revista.itson.edu.mx/index.php/rlrn/article/view/251
Rev Electron Vet	2017	Pt	IRT	N	N	Q4	---	https://www.redalyc.org/articulo.oa?id=63653009076
Rev Inv Vet Peru	2017	WA	P	Y	N	Q4	---	10.15381/rivep.v28.i2.13073
BsC Thesis UNMSM	2017	E, F, L	P	N	N	---	---	https://cybertesis.unmsm.edu.pe/handle/20.500.12672/8661
BsC Thesis UPCH	2017	E	P	N	N	---	---	https://repositorio.upch.edu.pe/handle/20.500.12866/1351
Rev Peru Biol	2018	E	P	Y	N	Q3	---	10.15381/rpb.v25i4.14312
Rev Peru Med Exp Salud Publica	2018	F	IRT	Y	Y	Q3	---	10.17843/rpmesp.2018.353.3737
Zoonoses Public Health	2018	L, WA	IRT	N	Y	Q1	Q1	10.1111/zph.12456
BsC Thesis UCSUR	2018	WA	P	N	Y	---	---	https://biblioteca.cientifica.edu.pe/cgi-bin/koha/opac-detail.pl?biblionumber=118
BsC Thesis UNC	2018	L	P	N	Y	---	---	https://repositorio.unc.edu.pe/handle/UNC/2725
PhD Thesis UNC	2018	Pt	P	N	Y	---	---	https://repositorio.unc.edu.pe/handle/UNC/2131
MsC Thesis UPCH	2018	E	P	N	Y	---	---	https://repositorio.upch.edu.pe/handle/20.500.12866/3854
Am J Trop Med Hyg	2019	E	IRT	N	Y	Q2	Q2	10.4269/ajtmh.18-0776
Rev Peru Med Exp Salud Publica	2019	H	IRT	Y	Y	Q3	---	10.17843/rpmesp.2019.363.4366
Sci Rep	2019	H	IRT	N	Y	Q1	Q1	10.1038/s41598-019-42423-3
Rev Inv Vet Peru	2019	L	P	Y	N	Q4	---	10.15381/rivep.v30i1.15670
Biotempo	2019	L	P	Y	N	---	---	10.31381/biotempo.v16i2.2528
Rev Inv Vet Peru	2019	Pt	P	Y	N	Q4	---	10.15381/rivep.v30i4.17263
BsC Thesis UNP	2019	E	P	Y	N	---	---	https://repositorio.unp.edu.pe/handle/UNP/1957
MsC Thesis UNT	2019	L	P	Y	N	---	---	https://dspace.unitru.edu.pe/handle/UNITRU/15313

PJ: Peruvian journal; PM: indexed in PubMed; WoS: Web of Science; Ref: Reference; Q: Quartile (considered that of publication year, in Web of Science only available for articles included in Science Citation Index Expanded; when the journal is listed in more than one category, the quartile indicated is the most favorable). H: Human, F. Food; L: Livestock; Pt: Pets; E: Environment; WA: Wild animals; P: All authors from Peruvian Institutions; IRT: International Research Team (manuscripts signed by authors from Peruvian and foreign institutions), when an author signed with double affiliation (Peruvian and foreigner) was considered as IRT; Y: Yes; N: No; NF: While indexed in SCOPUS, no data about the quartile was found in the SCOPUS webpage (information limited to the period 2011-2020). UNP: Universidad Nacional de Piura; UNMSM: Universidad Mayor de San Marcos; UPCH: Universidad Peruana Cayetano Heredia; UCSUR: Universidad Cientifica del Sur; UNT: Universidad Nacional de Trujillo; UNC: Universidad Nacional de Cajamarca

Table 2. Time from sampling to data publication.

Source [b]	Delay in Publication [a] Overall (30) N/n	Overall (30) Rg	Overall (30) Median	PM (10) N/n	PM (10) Rg	PM (10) Median	LJ/NPM (11) N/n	LJ/NPM (11) Rg	LJ/NPM (11) Median	TH (8) N/n	TH (8) Rg	TH (8) Median
Human	6/5	2-7	4.0	6/5	2-7	4.0	0/0	---	---	0/0	---	---
Aliments	3/2	2-7	4.5	2/1	7	7.0	0/0	---	---	1/1	2	2.0
Wild Animals	4/3	2-4	3.0	1/1	3	3.0	2/1	2	2.0	1/1	4	4.0
Environment	8/8	0-18	2.0	3/3	2-4	3.0	1/1	18	18.0	4/4	0-2	1.0
Livestock	10/9	0-5	3.0	2/1	3	3.0	5/5	2-5	3.0	3/3	0-2	2.0
Pets	5/3	1-5	2.0	1/0	---	---	3/2	2-5	3.5	1/1	1	1.0
Overall	30/27	0-18	3.0	11/10	2-7	4.0	11/9	2-18	3.0	8/8	0-4	1.0

N: All studies; n: Studies with sampling dates; Rg: Range. Range and mean measured in years. When a study analyzed samples collected in different years, the last year was considered for the delay in publication. When a sampling was analyzed in different studies, the first data published were considered to determine the delay in publication, and only this manuscript is considered in the Table.

a Time elapsed from the end of sample collection and publication date (measured in calendar years).

b When an article reported samples from 2 or more different sources it was included in all the appropriate source categories but was only counted once in the "overall" file.

These findings open the door to emphasize the need to reinforce the development of studies on antimicrobial resistance out of clinical settings, considering multidisciplinary and "One Health" approaches, in order to dispose of a complete and not biased panorama which allow us to design multidisciplinary policies to deal with this problem.

The main limitation of this study is the probable loss of manuscripts, suggested by the high number of texts in non-article format, because of non-inclusion in electronic repositories, the presence in non-searched repositories and/or the presence only in bibliotheca. Nevertheless, this limitation magnifies a common problem in some low- and middle-income countries, including those from the Americas, that is, the relatively low level of transformation of results into searchable texts. This finding may be related to different factors, including the economic costs inherent to the performance of scientific studies and the maintenance of a stable research structure, as well as socioeconomic or occupational factors resulting in a lack of time and/or expertise in adequate scientific writing of results, or language barriers to access publication in international journals[14,15]. In fact, it has been reported the precarious situation in Peru of scientific publications in other areas of knowledge (16). In any case, it is needed to highlight that a research study remains incomplete until a searchable document is produced, and thereby this is a key point to be promoted in the country.

While *E. coli* is probably the most studied microorganism because of its cosmopolitan distribution, it is needed to take into account that other microorganisms may also play a similar role as sentinels of "antibiotic exposure" of different sources and environments. In this sense, the development of studies centered on Gram-positive microorganisms might provide of information about levels of resistance of different classes of antimicrobial agents, as for instance glycopeptides, such as vancomycin, or streptogramins among other[17].

In summary, the number of publications reporting antimicrobial resistance levels in E. coli from non-human infections in Peru in the period 2009-2019 is scarce. Among the publications in this field, a relevant number include unpublished theses suggesting the need to develop efforts and strategies to enhance research output. An increase in publication rates is needed to dispose of a complete scenario about antimicrobial resistance levels outside clinical settings.

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