Research article

Collaborative scientific production of epilepsy in Latin America from 1989 to 2018: A bibliometric analysis

Cristian Morán-Mariños [a],[*], Josmel Pacheco-Mendoza [a], Tatiana Metcalf [b], Walter De la Cruz Ramirez [c], Carlos Alva-Diaz [d]

[a] Universidad San Ignacio de Loyola, Unidad de Investigación en Bibliometría, Lima, Peru
[b] Red de Eficacia Clínica y Sanitaria, REDECS, Lima, Peru
[c] Departamento de investigación, docencia y atención especializada en epilepsia, Instituto Nacional de Ciencias Neurológicas, Lima, Peru
[d] Grupo de Investigación Neurociencia, Efectividad Clínica y Salud Pública, Universidad Científica del Sur, Lima, Peru

ABSTRACT

Socioeconomic and cultural factors coupled with an inability to control many endemic and emerging diseases have resulted in a growing incidence of epilepsy cases in Latin America. This study aimed to analyze and describe scientific research output trends in epilepsy research for the period 1989–2018. Publications were extracted from Scopus indexed journals. Bibliometric analysis was used to analyze scientific output including number of annual publications, documents, and publication characteristics. A mapping analysis using VOSviewer software visualized collaborative network analysis, co-citation analysis, and keyword co-occurrence analysis. SciVal quantitatively analyzed distribution of countries, institutions, citation counts, *H*-index, and research collaborative partnerships. A total of 176507 records were initially retrieved after which 5636 were analyzed. Overall, an increasing trend for publication output was observed from 19 articles in 1989 to 342 in 2018; the number of publications significantly increased over the past 20 years (p = 0.0065). The majority of publications were original articles (74.4%). Brazil had the most scientific production (55.2%), followed by Mexico (15.4%) and Argentina (10%). Extra-regional collaboration was primarily with the United States, United Kingdom, and Canada; intraregional collaboration was low. The most common area of investigation by co-occurrences was "diagnostic research" (37.2%), with studies based on electroencephalography and nuclear magnetic resonance. Epilepsy research in Latin America has seen a steady growth with significant increases over the past 20 years. Brazil, Mexico, and Argentina are the most productive countries in the field collaborating primarily with extra-regional countries of high-income.

1. Introduction

Epilepsy is considered to be a global health problem affecting people of all ages. Although some types of seizures are more common in childhood than adulthood, research shows that incidence among elderly persons is significantly higher than in any other age group [1]. Furthermore, epilepsy carries an increased risk of developing a variety of medical, psychiatric, and cognitive disorders that can have a significant impact on functional status [2]. Research has also shown epilepsy to be more frequently seen in low- and middle-income countries (LMIC) for the year 2017 [3]. The Global Burden of Disease study 2016 reported epilepsy as the sixth most common debilitating neurological disorder [1], affecting an estimated 50 million people worldwide, of which 5 million are in the Latin American region [4, 5].

Burneo JG, et al. [6] reported for the year 2005 an average prevalence of 17.8 per 1000 persons in Latin America (LA), with Guatemala and Mexico as countries with the greatest prevalence; meanwhile *Debacq, et al.* [7] concluded neurocysticercosis as one of the principle causes of epilepsy in LA. However according to *Kaiboriboon K, et al.* [8] it is important to consider the socioeconomic and cultural level of each country, as the causal relationship between neurocysticercosis infection and the development of epilepsy is primarily found in poverty-stricken areas where ingestion of *T.solium* is common. Other causes of epilepsy are neurological infections, neonatal encephalopathy, head-trauma, and cerebral tumors [7].

Given the importance of this disease in LMICs as in LA, it is important to analyze scientific production trends. A bibliometric analysis is a method that allows to measure scientific productivity in multiple fields, such as type of document, geographical and institutional distribution, and citation rate [9]. Studies indicate that scientific production on epilepsy in Latin America can be rare, as has been shown by *Park KM, et al.* where Brazil was identified as the country with the highest volume of scientific production levels in South America on epilepsy [10] yet smaller and less well funded countries, such as Haiti and Dominican Republic, have produced significantly less scientific output. A shift of scientific production is seen through increased international collaboration and expansion of institutional research capacity.

This study aims to analyze and describe trends on the scientific production of epilepsy research in LA, between 1989 and 2018. Secondary objectives include graphically representing the corresponding collaborative networks and identifying the most common areas of research.

2. Methods

2.1. Study design

We conducted a bibliometric analysis using documents published between 1989 and 2019 in Scopus indexed journals. We selected 1989 as a start date given that the International League Against Epilepsy (ILAE) [11] put into effect modifications of the 1981 classification, taking into account widely used of clinical features of epilepsy including: classification of epileptic seizures (combined generalized or focal and unknown); addition of neuroimaging and electroencephalographic studies to distinguish between idiopathic, cryptogenic, and symptomatic etiologies. This classification was applied in 2013 and 2017 keeping the general clinical characteristics of the groups [12].

2.2. Source of information

We chose Scopus (Elsevier BV Company, The Netherlands) as the electronic database to identify studies as it is considered to be the most comprehensive index of multidisciplinary literature worldwide including 100% of those indexed in Medline [13]. We did not use reference lists of articles.

2.3. Search strategy

We identified publications indexed in the Scopus database. A paper on epilepsy in LA was defined as having at least one author with a Latin American country affiliation. The search strategy included Medical Subject Heading (MeSH) terms for "epilepsy". Publications were limited to original research articles, review articles, letter, note, conference paper, short survey, editorial and erratum. For the complete and final search strategy, please refer to Supplementary material 1. A flowchart of the bibliometric search is shown in Figure 1. The period of publication dates was restricted from 1989 to 2018 and to English, Spanish, and Portuguese language only.

2.4. Data analysis

Data was imported to Microsoft Excel 2019. The analysis was divided into two stages: 1) data analysis between 1989 and 2018 using VOS viewer, and 2) data analysis between 2009 to 2018 using SciVal.

The first data analysis (1989–2018) resulted in annual production results (as compared to the Web of Science database), scientific production per country, type of publication, and journal metrics. Network visualization maps using VOSviewer version 1.6.6 (Leiden University, Leiden, Netherlands) were created in order to conduct a co-occurrence analysis of collaboration country and search terms. Graphic interpretation is based on the size of the circle, thickness of the connection lines, and distance between items (countries or keywords). The size of the
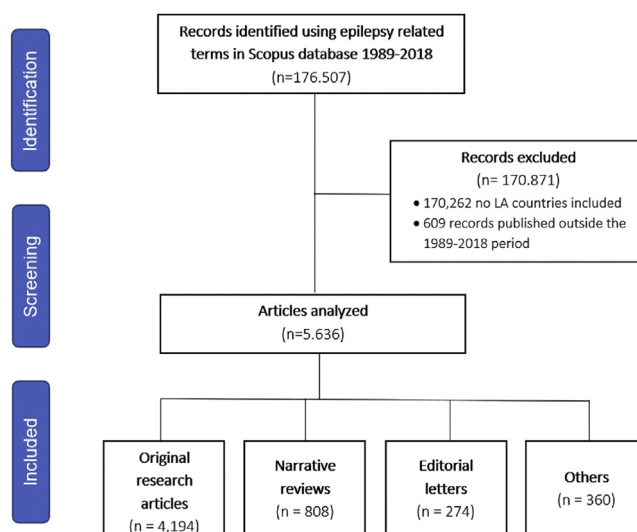

Figure 1. Flowchart of search strategy.

circle is dependent on the weight of the item – in our case, the total number of occurrences or productivity; the color of an item depends on the related cluster group; the thickness of the line is related to the strength of the link between items; distance is related to the number of co-occurrences between two terms where, in our study, close proximity between items indicates a strong collaboration [14].

The second analysis (2009–2018) used SciVal [15], an online tool that utilizes bibliometric information retrieved from Scopus allowing us to visualize research performance, identify collaborative networks, and analyze research trends. It provides a variety of metrics such as: publication by field, number of publications by institutions, and list of authors with the greatest number of scientific productions. Scopus also provides top articles with the most number of citations and percentage of scientific collaboration including national (country-level), international (extra-regional), and institutional partners (Supplementary material 2).

The bibliometric indicators used were: 1) scientific activity and distribution by years, calculated by the number of annual publications with at least one author affiliated with any LA country; 2) collaborative networks, represented by the percentage of international, national, and cross-institutional collaboration; 3) journal impact metrics, calculated by the number of citations and "Scholarly Output"; and 4) journal impact, through Scopus metrics and "SCImago Journal & Country Rank" extracting data such as the "SCImago Journal Ranking (SJR)", Quartile Scores, and CiteScore [16, 17].

Papers were then classified into research areas as identified by the search terms with the highest number of co-occurrences in epilepsy. A minimum of 20 occurrences for each term were used.

2.5. Ethics

The data were downloaded from available published research, thereby no ethics approval was required.

3. Results

Our initial search yielded 176507 publications after which 5636 publications were analyzed (Figure 1). The average annual publication of articles on epilepsy in LA was 180 articles per year, with an annual increasing rate of 15.8%; a Web of Science database comparison showed a similar trend (Figure 2).

In the last two decades (1999–2018), there was a significant increase up to 4.2 times greater in scientific production (p = 0.0065) with respect
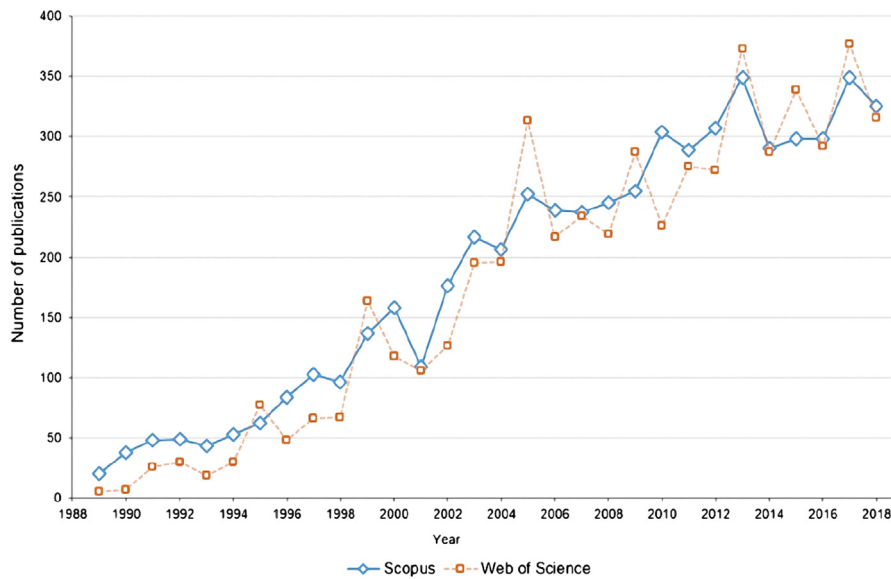
Figure 2. Trends in the scientific production of Latin American countries on epilepsy: 1989–2018.

Table 1. Publication years and types of journal articles.

Year	Documents	Original Research	Review Articles	Letter	Others*
1989–1993	198	180	11	3	4
1994–1998	398	331	23	9	35
1999–2003	797	614	98	13	72
2004–2008	1179	858	197	43	81
2009–2013	1504	1082	221	110	91
2014–2018	1560	1129	258	96	77
Total	5636	4194 (74.4)	808 (14.4)	274 (4.8)	360 (6.4)

Others*: Conference Paper, Note, Editorial, Short Survey, Erratum.

to 1989 and 1998. The majority of publications were original articles (n = 4,194; 74.4%) and reviews (n = 808; 14.3%) (Table 1).

The five countries with the most production in LA were: Brazil with 3272 reports (58%), followed by Mexico (913; 16.1%), Argentina (596; 10.5%), Colombia (231; 4.1%) and Cuba (230; 4.1.%); meanwhile the rest of the countries had less than 200 documents published (394; 7%) (Figure 3). Brazil had an annual increase rate of 18.3%, followed by Argentina with 13.5% and Mexico with 11.1%.

We identified 21 journals with a minimum of 30 publications between 1989 and 2018; four were from LA. The top journals included
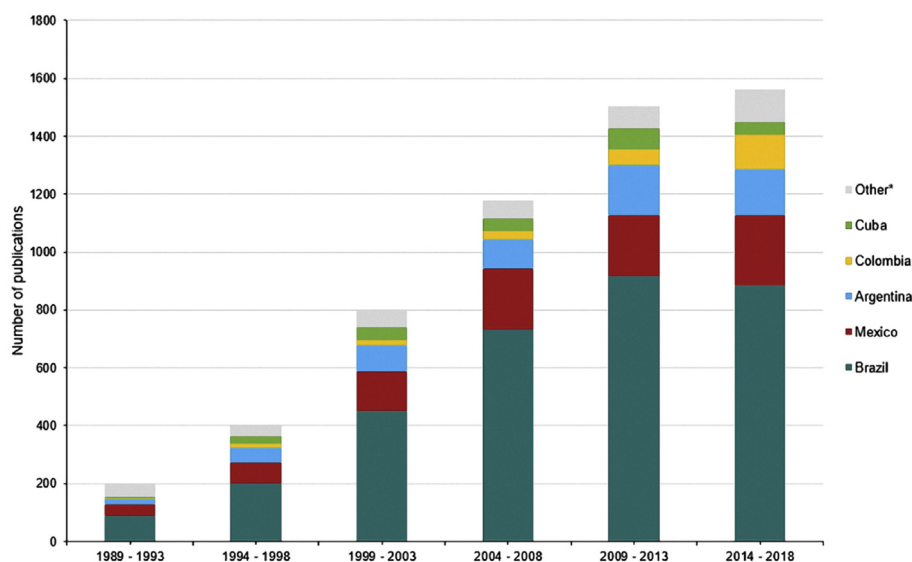

Figure 3. Epilepsy publications per four-year increments, stratified by Latin American countries: 1989–2018. *Other: Countries with less than 200 publications.

"Arquivos de Neuro-Psiquiatria" with 510 (10%) publications, followed by "Epilepsy and Behavior" and "Epilepsia" with 412 (7%) and 340 (6%) number of publications, respectively. In 2018, journal rankings were as follows:

- The country with the greatest Quartile Score (Q1 quartile) was the USA, meanwhile the remaining journals belonging to LA were of lesser impact (Q4 = ¾ and Q3 = ¼).
- The most cited neurology journal was "Neurology"; it achieved the highest SJR (3.502). Whereas "Epilepsia" ranked as the most cited with an average of 5.11 citations per article, according to CiteScore.
- The journals with the highest and least percentage of international collaboration were "Revista Ecuatoriana De Neurologia" (40.91%) and "Revista De Neurologia" (8.6%) (Table 2).

Extra-regional collaborations were primarily with the USA, UK, Canada, Italy, and Germany (Table 3). Haiti and the Dominican Republic produced a total of less than 5 articles, Paraguay did not publish any article on epilepsy, according to Scopus. Collaborative networks required a minimum of 20 publications per country. Brazil and Mexico had the greatest collaborative networks with 32 countries, followed by Argentina (31), Chile (29) and Uruguay (25). Venezuela (13) and Puerto Rico (4) were the countries with the least collaboration; intra-regional collaboration among LA countries was low (Figure 4).

There were 90 out of 15758 keywords that were utilized in 5636 documents and that had a minimum of 20 occurrences. These were then organized and presented into clusters as determined by the total number of occurrences (Figure 5). *Cluster 1:* Diagnostic research (12413 occurrences; 37.2%); *Cluster 2:* Treatment research (7,051 occurrences; 21.1%); *Cluster 3*: Other (8086; 24.2%); *Cluster 4:* Causes (5775; 17.3%).

There were three communal areas: diagnostic, treatment, and causes. Whereby "Diagnostic research" was the most common, where the majority of documents that discuss about electroencephalography and magnetic nuclear resonance (MNR). The documents about "Treatment research" investigated themes about anticonvulsive medications where valproic acid and carbamazepine were the most studied. Studies on the "Causes" of epilepsy focused on the etiology of convulsions. Unlike other research carried out in this area, we found a large majority of studies focused on both adolescence and adulthood.

We analyzed 3064 documents in the period from 2009 to 2018 with SciVal. Results showed that the subject area with the most publications was Life Sciences & Medicine; medicine, biological sciences, and pharmacology were the subcategories most studied. The most prolific institutions included: Universidade de Sao Paulo (n = 548), Universidade Federal de Sao Paulo (n = 460), and Universidade Estadual de Campinas (n = 203). Other relevant non-Latin American institutions were the University College London (n = 88) and Harvard University (n = 76). Of the top 10 authors with the most research publications on epilepsy (publications >50 documents) nine were from Brazil and one from the USA. We identified 386 documents affiliated with LA that were ranked within the top 10% of publications most cited worldwide. Our findings identified international research

Table 2. Top journals with the most commonly published articles on epilepsy research in Latin America, 1989–2018.

| Journals	Number of articles (%)	Quartile Scores[a]	CiteScore 2018[¥]	SJR 2018[¥]	% International collaboration (2018)[a]
Brazil					
Arquivos De Neuro Psiquiatria	578 (10%)	Q3	0.87	0.487	14.71
Journal of Epilepsy And Clinical Neurophysiology*	288 (5%)	discontinued			
Brazilian Journal of Epilepsy and Clinical Neurophysiology*	58 (1%)	discontinued			
Mexico					
Revista Mexicana de Neurociencia	46 (1%)	Q4	NA	not assigned	NA
Archivos de Neurociencias	36 (1%)	Q4	0	0.100	23.53
Ecuador					
Revista Ecuatoriana de Neurologia	40 (4%)	Q4	0.14	0.119	40.91
United States					
Epilepsy and Behavior	412 (1%)	Q1	2.48	1.3	19.48
Neurology	77 (1%)	Q1	3.85	3.502	19.31
Epileptic Disorders	56 (2%)	Q2	1.94	0.823	39.47
Journal of Child Neurology	39 (1%)	Q1	1.90	0.973	10.08
PLoS One	37 (1%)	Q1	3.02	1.1	33.01
United Kingdom					
Epilepsia	340 (6%)	Q1	5.11	2.85	36.30
Seizure	145 (3%)	Q1	2.77	1.172	24.90
Spain					
Revista de Neurologia	256 (5%)	Q3	0.38	0.199	8.60
Neurologia Argentina	38 (1%)	Q4	0.04	0.106	10.00
Netherlands					
Epilepsy Research	177 (3%)	Q2	2.36	0.963	22.83
Brain Research	55 (1%)	Q1	3.15	1.364	22.25
|Neuroscience Letters	44 (1%)	Q3	2.21	0.858	20.16
Pediatric Neurology	36 (1%)	Q1	1.82	0.907	13.37
Clinical Neurophysiology	33 (1%)	Q1	3.14	1.634	31.30
Germany					
Child's Nervous System	36 (1%)	Q2	1.16	0.492	16.80

* Journal of Epilepsy And Clinical Neurophysiology previously known as Brazilian Journal Of Epilepsy And Clinical Neurophysiology in 2001, Scopus discontinued it in 2012.

a Source: SC imago Journal & Country Rank(2018).

¥ Source: SCOPUS(2018).

Table 3. Extra-regional countries with most scientific collaboration with countries of LA.

Extra-regional countries	N of documents	% collaboration
USA	732	12.987
UK	262	4.649
Canada	242	4.294
Italy	202	3.584
Germany	198	3.513

*Eleven countries in Latin America with a minimum of 20 publications in Scopus
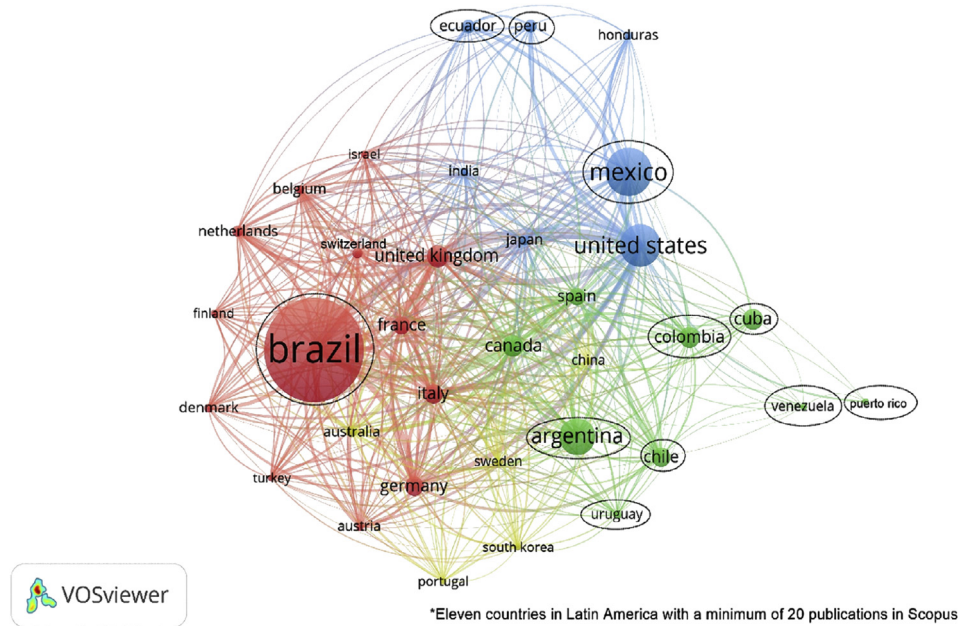
Figure 4. Extra-regional collaborations on epilepsy research. We required a minimum of 20 documents and included 25 countries.
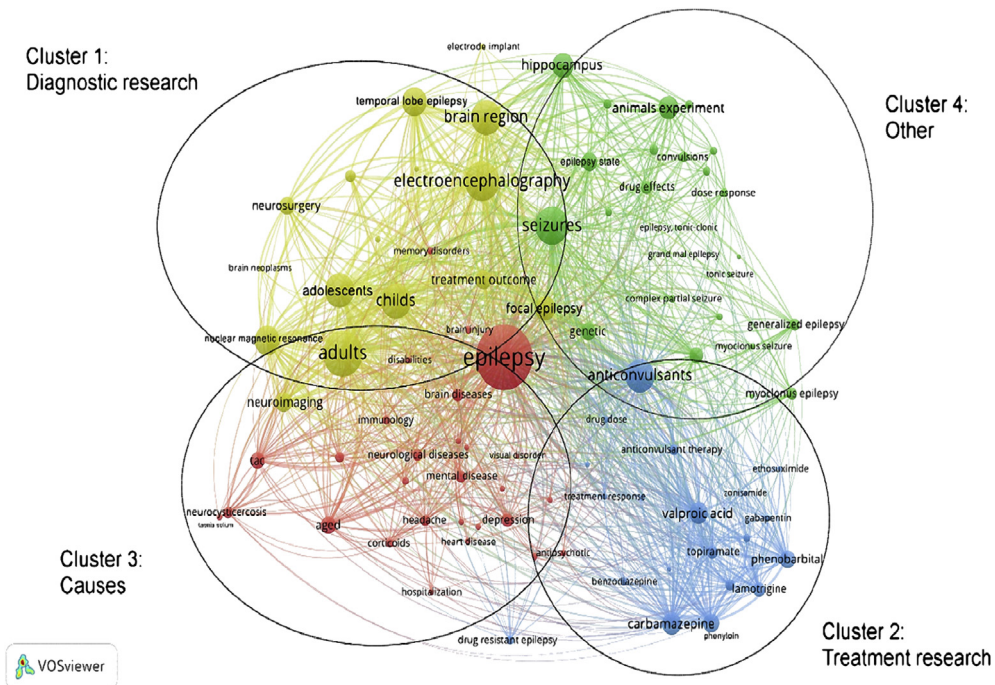
Figure 5. Co-occurrence network of keywords map. The size of the circles is scaled according to the number of total occurrences of each term. The lines between each term indicate co-occurrence. A minimum of 20 occurrences for each term were used; the map displays 90 words.

collaboration in 34% of publications; whereas collaborative research in-country was 20% (Supplementary material 2).

4. Discussion

The last two decades have seen a rapid increase in the scientific production of epilepsy in Latin America with Brazil, Mexico, and Argentina as the three most prolific nations. Moreover, these are the same countries that had the most international collaboration in the period between 2009 and 2018, mainly with the United States, United Kingdom, and Canada. The majority of the scientific production were original articles, with electroencephalography and seizures being the most common topics.

Our study found scientific production in LA to be related to the amount of funding it receives in the R&D sector. From 2004 to 2013, the 126% increase in scientific production was attributed to increased funding oriented towards research teams [18] as evidenced by: 1.) a rise in scientific output by universities and research institutions, 2.) an increased number of hospitals with highly specialized care facilities, and 3.) an enhanced level of international collaborations similar to those formed and maintained by Brazil, Mexico, and Argentina. We believe the latter to be one of the main factors on impact and quality of scientific output emerging from these three countries, in comparison to the rest of LA [19]. Mainly, Brazil has shown to explore different fields of clinical research and with great external support, this could mean an opportunity for countries with lower scientific production to develop greater intra-regional collaboration with Brazil [20, 21].

Furthermore, high-income countries, such as the United States, Canada, and United Kingdom spearhead the development of alternative treatments for epilepsy - including comprehensive epilepsy programs [22, 23]. Up to 34% of epilepsy research from high producing LA countries can be attributed to international collaboration with high-income countries [24].

Low scientific output in countries like Haiti and the Dominican Republic may be partly explained by the low levels of collaboration and decreased research funding in their respective country [18]. We did not find any cited articles on epilepsy research in the Scopus database for Paraguay, this lack of epidemiological data on epilepsy has also been confirmed by local ILAE members [25]. Low levels or even lack of production in countries not only affects indicators that measure scientific growth, but also the ability to precisely estimate the prevalence and impact of this disease at country level. Without such metrics, countries will likely experience near-term or long-term effects and ramifications in the planning of public health policies. In April of 2019, and in response to this situation, the LA regional chapter of the ILAE conducted capacity building sessions on scientific, social, and cultural issues in order to promote education and awareness about epilepsy and highlight the need to develop specialized treatment centers as well as advancing medical research [26]. Experiences of LMICs, like that of Iran, that show strengthening of scientific collaborations resulting in an progressive increase of scientific production with greater visibility and impact on epilepsy research demonstrate that building successful collaborations is not only feasible but key to improving output [9].

4.1. Link between scientific output and national burden of epilepsy

The scientific production on epilepsy in LA is higher than other neurological diseases, even those with higher prevalence - such as stroke, producing an average of 164 articles per year from 2003-2017 [24] or those with constant innovation in treatment therapy - such as multiple sclerosis, with an average of 115 articles per year from 1996 – 2010 [27].

Epilepsy is a global disease where 80% of affected individuals reside in developing countries including those found in LA [6, 28]. It is evident that not only is there a higher prevalence (17.8 per 1000 people) or incidence (77.7–190 per 100000 people per year) of epilepsy in LA but also an inequality in treatment distribution and access to public health services than in high-income countries.

Epilepsy can have a variety of different comorbidities such us depression, migraines, and sleep disorders which could have a negative impact on both quality of life and life expectancy [29, 30, 31]. For this reason, the ILAE from 2014 to 2020 agreed on the need to maintain and formulate clear policies to improve research, collaboration and financing for this disease [32, 33]. This might explain the growing trend of publications seen in the last four years of the study period (2014–2018).

4.2. Link between scientific output and Latin American demographics

LA is a region comprised of countries of low- and middle-income reporting significantly higher prevalence and incidence on epilepsy as compared to high-income countries [34]. This increased prevalence and incidence coincides with our findings of an increased scientific production on epilepsy in the region over the last couple of decades. As Latin American demographics continue to escalate, as does its aging population, there is continued evidence that the majority of the prevalence is found in elderly populations. These issues pose a challenge that when combined with the association of age-related cerebrovascular, neoplastic, and neurodegenerative disorders emphasizes the need for ongoing investigations [35]. Given this data, it is therefore important to continue to carry out investigations on epilepsy, particularly in vulnerable elderly populations that they might be misdiagnosed (present with conditions that can mimic epileptic seizures) or fail to receive opportune medical treatment. Furthermore, understanding the role of these risk factors for proper complications and treatment is important for developing clear and effective strategies for improving epilepsy [36].

4.3. Link between scientific output and clinical outcomes

Our findings indicate that scientific production on epilepsy in LA countries focuses primarily on therapeutics, diagnostics, and etiology of the disease. However, research is still lacking in areas evaluating treatment gap, low adherence or pharmacoresistance to anti-epileptic drug therapy [37, 38], and in addressing diagnostic difficulties in distinguishing other medical conditions from seizures, as with imitators of epilepsy [39, 40].

As expected, patients showing non-compliance with therapy or who fail to take their anti-epileptic drugs will have a poor clinical outcome. Similarly, patients who are not properly diagnosed or there is a large treatment gap due to low socioeconomic status strongly predict poor clinical response. We also believe that an improved prognosis may be achievable by evaluating medical conditions that might lead to an increased risk for seizures, particularly those well-known and often inevitable in the region such as obstetric complications, perinatal factors, parasitic infections, and traumatic stress disorder [41], as well as those of unknown etiology. Likewise, epidemiological studies on the burden of epilepsy, risk factors involved, and studies on the economic impact of epilepsy in Latin America are important in the planning and distribution of health services.

4.4. Implications and limitations

Our bibliometric study was limited to journals indexed in Scopus, where other journals may have not been included as a result. Notwithstanding, it is important to note that Scopus has clear advantages in terms of precise citation results and is considered to be one of the largest citation database of peer-reviewed literature [13]. Although our search strategy was an exhaustive one for the word "Epilepsy", we were unable to exclude the term "Seizure" given that recurring seizures form part of the definition of epilepsy, hence our search not only represents studies based solely on "Epilepsy" but also on "Seizure". Finally, the VOSviewer software is unable to calculate a statistical relationship, yet it allows for visualization of links between items.

5. Conclusions

Scientific production on epilepsy in LA continues to grow, but still faces many challenges. The largest production comes from Brazil, Mexico and Argentina - countries that collaborate with extra-regional high-income countries such as the United States, UK, and Canada. In LA the research topics are focused on "Diagnostic research", this could imply that the other areas may be little explored. It is necessary to strengthen integration between LA countries, because it could be detrimental by limiting access to complementary knowledge. In addition to the creation of extra-regional networks, this document supports the idea that countries with greater scientific production could have had capacity development or institutional strengthening through financial incentives designed to acquire or improve existing research capacities. The rapidly changing demographics, political instabilities, and socioeconomic characteristics create enormous challenges for conducting epilepsy research, especially in resource poor settings. We hope that our research will be valuable in highlighting the need for continued epilepsy research in Latin America including the need for increased intra-regional collaboration and effective implementation of services to improve patient outcomes and respond to the challenge of epilep.

Declarations

Author contribution statement

Cristian Morán-Mariños, Josmel Pacheco-Mendoza: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Tatiana Metcalf, Walter De la Cruz Ramirez, Carlos Alva-Diaz: Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

Data included in article.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

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