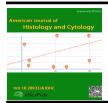
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Research on Brain Tumors in Mexico: A Bibliometric Analysis from Latin America

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ABSTRACT

Background: Bibliometrics is a completive method of research and analyses useful to understand the collective contributions of a given scientific community. The detail of the quantity (productivity) and impact as a surrogate marker of quality can shed light on what we have done (number of articles) and how we impact others (citations). It also shows the direction the community can take for further research, guided by its shortcomings and successes. The publications of Latin American medical institutions on brain neoplasms have never been studied. Objective: Analyze a clinical and experimental approach, identifying core journals, type of article, increase of published material with time, number of citations. Additionally, we identified the most researched topics involved in brain tumor literature. Material and methods: We harvested the articles published by at least one author from the Instituto Nacional de Neurología y Neurocirugía from Mexico from its inception in 1964 to 2020. Key bibliometric parameters, as the journal of publication, type of paper, number of articles, and citations were recorded. Results: In cerebral neoplasms, our institution produced 291 articles (clinical versus experimental: 227 vs. 64). With a modest productivity before 2000, the production had increased 8-fold by 2019. The main topic is glioblastoma, also with the highest number of citations. Researchers prefer to conduct original investigations rather than subject reviews. Most papers were published in Archivos de Neurociencias (institutional journal produced in Spanish), most papers published in English were in the Journal of Neuro-Oncology. Discussion: Productivity had an encouraging growth in the last decade, but more emphasis should be given to target international journals, which offer a high number of readers and citations. Strategies to reach these goals have to be found and should be implemented. Conclusion: Research on brain tumors in Mexico has recently shown buoyancy and we should profit from this inertia to give a definitive boost to it, which might benefit authors and institutional prestige. But mainly, with a more robust research, we could find better solutions for our patients, applicable in the national and international context.

Keywords: Bibliometric, México, Gliomas, Meningiomas, Medulloblastoma.

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Introduction.

Bibliometric studies are used to evaluate various grouped investigations parameters of Scopus, Journal Citations Reports, and Google Scholar are repositories, with different methodologies, studying the productivity and impact to compare institutions in order to guide topic research [2], and find areas for improvement and cooperation. Our institution, the Instituto Nacional de Neurología y Neurocirugía (INNN), is one of the main referrals centres for cerebral neoplasms in Latin America, but topics in the collective mind of authors and topics of interest have not been studied. Brain tumours are the tenth leading cause of death in the world [3]. Last year, among leading causes of death in Mexico, malignant tumours ranked fourth [4]. However, specific statistics on brain neoplasms are unknown, and extrapolations from two institutional series 50 years apart [5,6], estimate an incidence of 3,5 cases per 100,000 (around 4,410 annual cases). In the UK, intracranial and other CNS tumours are the 9th most common cause of cancer-related death, accounting for 3% of all cancer deaths in 2018^[7].

No bibliometric analysis on brain tumour research has been performed in Latin America and regional and national statistics are generally limited to institutional series. Both facts underline the gap we pretend to fill with this bibliometric analysis of one of the largest Latin American institutions dealing with brain tumours. This will encourage, we hope, national and regional initiatives for joint efforts to start national registries of incidence and cooperative studies between countries with similar health problems. We can then find areas which could be improved, and where we should focus our efforts in the years to come.

Material and methods.

The main corpus was harvested from Scopus on January 1st, 2021, restricted to a single affiliation (ID: 60000029, Instituto Nacional de Neurología y Neurocirugía) from 1964 to 2020 and we selected those related to brain tumours. We

sorted them according to the main topic (type of tumour) and to avoid duplications, every article was classified into a single category. As with our previous bibliometric studies [8,9,10], we considered for analysis: topic, year and journal of publication, country and impact factor of the journal, document type, research area (clinical or basic), number of papers per year, citations and pattern of collaboration (endogamic, national or international participation). Only descriptive statistics were performed.

Results.

From an institutional production of 3,032 papers, roughly one in ten (291) were related to cerebral neoplasms: 227 clinical and 64 experimental, yielding a clear dominance of clinical studies (78%) (Figure 1). During the first decades of publication history, brain tumours were not a priority in institutional research and the relevant "take-off" can be traced to year 2000. For comparison around that pivotal year, the number of papers jumped from 15 to 212 in the clinical field and from 7 to 57 in basic research. Since then, production has been uneven, and topped at 24 papers in 2019. (Figure 2). This positive upward trend is encouraging and was observed in both areas (clinical and experimental) (Figure 3). In the group of 227 clinical articles, 193 were original, 14 reviews, 10 letters, six conference papers, and four book chapters (Figure 4). In the 64 experimental, 54 were original, five reviews, and five conference papers.

A few journals publish the majority of our research, the top 9 are summarized in table 1. The percentage of papers hosted by our domestic journal "Archivos de Neurociencias" is 41% and 15% the "Journal of Neuro-Oncology". Clinical and experimental studies are evenly split Archivos de Neurociencias. Various experimental articles were published international journals (BioMed Research International and British Journal Cancer, each one has roughly 20%), the top 6 journals for experimental research are shown in Figure 5.

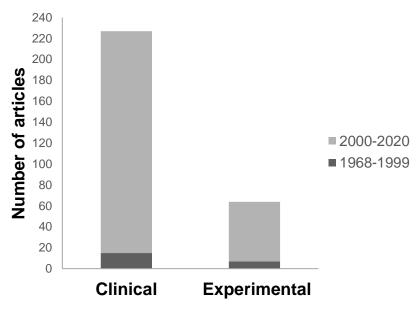


Figure 1. Clinical and experimental articles. INNN has produced 291 articles related to tumors since its foundation in 1968 to 2020, of which 227 correspond to the clinical aspect and 64 to the experimental one. From clinical articles, 15 were published between 1968-1999 and 212 between 2000-2020. From experimental articles, 7 were published between 1968-1999 and 57 between 2000-2020.

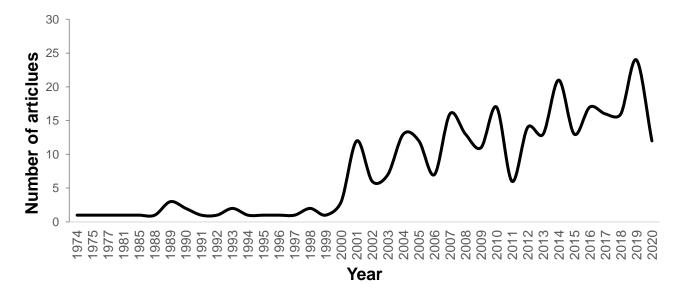
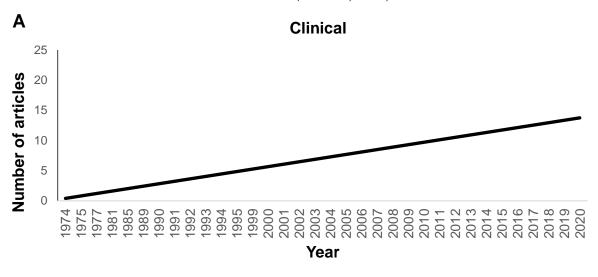


Figure 2. The number of articles published per year related to tumors, with a very notable increase from 2001 and a maximum peak in 2019 with a total number of 24 articles.

Table 1. Journals with the most tumours-related research. "Archivos de Neurociencias" lead the list with 40.9% of the articles from this journal, following "Journal of Neuro-Oncology" with 15.1%.

Journal	Percentage of articles
Archivos de Neurociencias	41
Journal of Neuro-Oncology	15
Gaceta médica de México	9
Revista de Neurologia	9
Annals of Diagnostic Pathology	5
Cirugia y Cirujanos	5
Journal of Neurosurgery	5
Surgical Neurology	5
World Neurosurgery	5



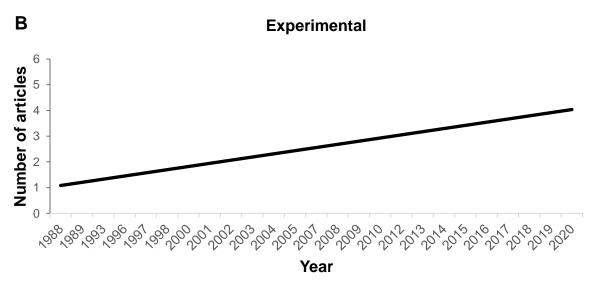
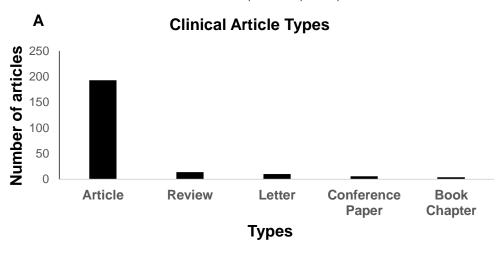


Figure 3. Tendency of published articles. The tendency of published articles has been increasing over the years, both in clinical (A) and experimental (B) articles.

Table 2. The ten most cited articles. From the 291 articles related to tumours produced by the INNN, the most cited had 297 citations up to the time of the review.

Institute	Article	Year	Citations	Journal
INNN	Adding chloroquine to conventional treatment for glioblastoma multiforme: A randomized, double-blind, placebo-controlled trial	2006	297	ANNALS OF INTERNAL MEDICINE
INNN	CpG island hypermethylation of the DNA repair enzyme methyltransferase predicts response to temozolomide in primary gliomas	2004	221	CLINICAL CANCER RESEARCH
INNN	Angiotensin II, cell proliferation and angiogenesis regulator: Biologic and therapeutic implications in cancer	2004	117	CURRENT VASCULAR PHARMACOLOGY
INNN	Cas Ilgly induces apoptosis in glioma C6 cells in vitro and in vivo through caspase-dependent and caspase-independent mechanisms	2005	97	NEOPLASIA
INNN	Study of the stabilization of zinc phthalocyanine in sol-gel TiO2 for photodynamic therapy applications	2010	95	NANOMEDICINE: NANOTECHNOLOGY, BIOLOGY, AND MEDICINE
INNN	Institutional experience with chloroquine as an adjuvant to the therapy for glioblastoma multiforme	2007	87	SURGICAL NEUROLOGY
INNN	Blockage of angiotensin II type I receptor decreases the synthesis of growth factors and induces apoptosis in C6 cultured cells and C6 rat glioma	2005	83	BRITISH JOURNAL OF CANCER
INCAN	Effects of an oral nutritional supplement containing eicosapentaenoic acid on nutritional and clinical outcomes in patients with advanced non-small cell lung cancer: RANDOMISED trial	2014	81	CLINICAL NUTRITION
INNN	Therapy of glioblastoma multiforme improved by the antimutagenic chloroquine.	2003	78	NEUROSURGICAL FOCUS
INNN	AT1 receptor is present in glioma cells; its blockage reduces the growth of rat glioma	2001	77	BRITISH JOURNAL OF CANCER



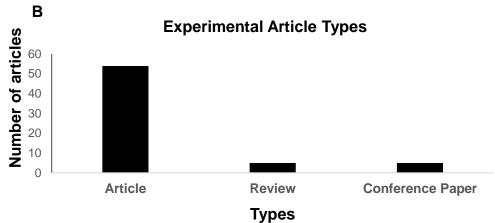


Figure 4. Article types. A) Among the 227 clinical articles, there are 193 original articles, 14 reviews, 10 letters, 6 conference papers and 4 book chapters. B) Among the 64 experimental articles, there are 54 original articles, 5 reviews and 5 conference papers.

Table 3. A) The authors from the INNN and others affiliations which contributed the most in tumours-related clinical and experimental research. B) The principal corresponding authors that have worked on clinical and experimental tumours-related research at the INNN and other affiliations in Mexico. INCan: Instituto Nacional de Cancerología. UAM: Universidad Autónoma Metropolitana.

CLINICAL		
A) 1st author	Percentage of articles	From
Tena-Suck M.L.	8	INNN
Cacho-Díaz B.	2	INCan
Aguirre-Cruz L.	2	INNN
B) Corresponding author	Percentage of articles	From
Tena-Suck M.L.	13	INNN
Arrieta, O.	3	INNN / INCan
Portocarrero-Ortiz, L.	2	INNN
S EXPERIMENTAL		
A) 1st author	Percentage of articles	From
López T.	13	INNN / UAM – Xochimilco
Arrieta O.	6	INNN / INCan
Sotelo J.	5	INNN
B) Corresponding author	Percentage of articles	From
Pineda, B.	13	INNN
Arrieta, O.	9	INNN / INCan
Sotelo, J.	8	INNN

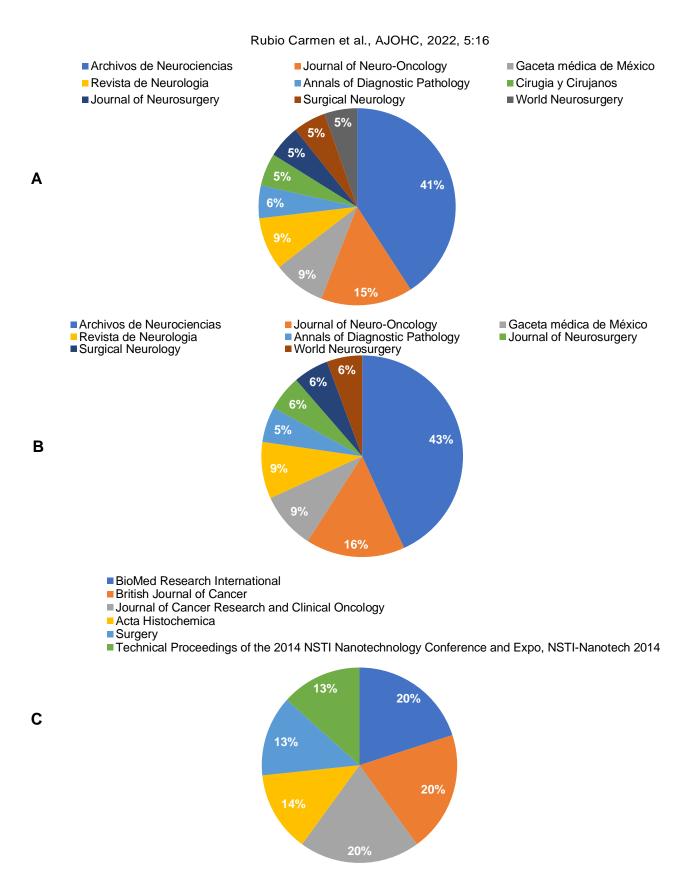
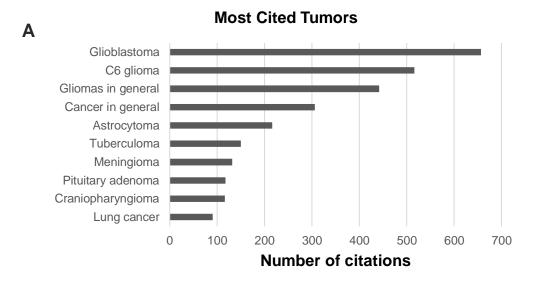
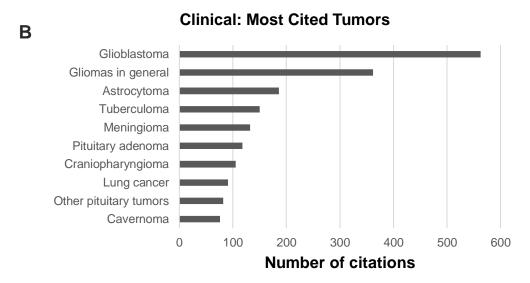


Figure 5. Preferred journals for publication. A) Main journals that have published INNN articles related to tumors, headed by the journal "Archivos de Neurociencias", with 41% of the articles published by these journals. B) Main journals that have published clinical articles of the INNN related to tumors, headed by the journal "Archivos de Neurociencias" with 43% of the articles published by these journals. C) Main journals that have published INNN experimental articles related to tumors, headed by the journals "BioMed Research International" and "British Journal Cancer", with 20% of the articles published by these journals each one.





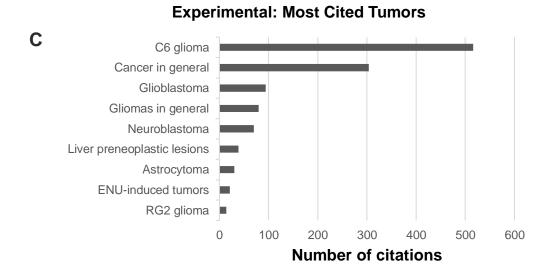


Figure 6. Most cited tumors. A) The 10 types of tumors in both clinical and experimental articles with the highest number of citations, headed by glioblastoma with a total number of citations of 657. B) The 10 types of tumors in clinical articles with the highest number of citations, headed by glioblastoma with a total number of citations of 563. C) The 10 types of tumors in experimental articles with the highest number of citations, headed by C6 glioma with a total number of citations of 516.

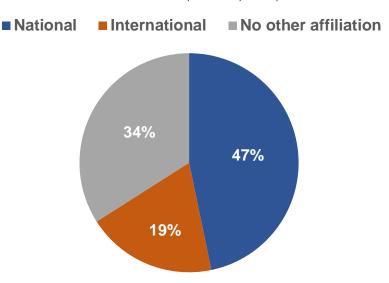


Figure 7. Affiliation types. From 291 articles related to tumors with the INNN as their affiliation, only 19% had international affiliations, while 47% had national affiliations and 34% had the INNN as their only affiliation.

Glioblastoma is the front-runner with 657 citations of 27 papers, (563 citations for clinical / 94 citations for experimental) (Figure 6). The top-paper (297) was published in 2006 in *Ann Intern Med*: "Adding chloroquine to conventional treatment for glioblastoma multiforme: A randomized, double-blind, placebo-controlled trial" (Table 2). The proportion of articles that did not receive a single citation (L0 index) was 34% (100 out of 291).

Cooperation patterns for an institution are important and may guide future projects, with bibliometric analysis highlighting the collective interest of a group of researchers. It seems that in brain tumours, it seems that Mexican researchers are not prone to collaboration: 34% of the papers were home-authored, 47% has external national participation, and a meagre 19% of them had international collaboration (Figure 7). The most successful corresponding authors had joint projects with national research facilities like the Instituto Nacional Cancerología (INCAN) or the Universidad Autónoma Metropolitana (UAM) (Table 3).

Discussion.

No national statistics are available for the incidence of brain tumours, and this clearly shows that this pathology has been neglected by

medical research. But all Latin American countries experience this problem, as described by Contreras in 2017^[11]. This perfectly explains why the Instituto had a modest production before year 2000, and our study shows that this situation is changing, as there is a growing interest on the subject. As previously said, no Latin American country has a national registry of brain tumours, and their precise incidence is unknown and is only inferred from mortality statistics and institutional discharge numbers. Our paper is a call to action for oncologists, neurosurgeons and other stakeholders to start epidemiological studies at a regional level.

The ratio clinical versus basic is four to one in publications. According to Science [12], in Mexico, research and development budget accounts for 0.46% of the GDP (60% and 87% less than Brazil and Japan respectively). For experimental studies the inoculation of tumour cells into animals requires a budget and infrastructure suitable to generate original results worth being published.

Clinical studies can be performed with the patients who are being already cared for in a national referral centre such as the INNN and often require little additional budget. The value of clinical case series is unquestionable, as

observational designs in our countries with limited resources, may reveal patterns not reported in the literature authored in more developed countries, due to ethnic, social or infrastructure differences. For example, Mexican patients can hardly afford chemotherapy (out of pocket expense), while in Western Europe social security grants access to this treatment. Therefore, some patients have to be treated outside the international guidelines [13], because they cannot afford optimal therapy or adequate molecular markers of methylation status typing. What happens to these patients, who might be underrepresented in foreign literature (European or American)? This is a pertinent question which can be answered in prospective international studies.

Archivos de Neurociencias is the institutional journal, whose first issue dates 1986 and hosts 41% of the scientific production in tumours. No clear interpretation of this can be given, as we do not have statistics about what is the normal percentage of articles that are published in domestic journals and consequently what proportion can be sent to a foreign publication with reasonable possibilities of being accepted.

But let's stop a few moments and consider what happens to a research project not conceived in the top universities or hospitals or developed countries:

First, I conceive the idea in my mind. Second, I design the plan, carry out the experiment, analyse and interpret the data and write the manuscript. Up to this point, no else than the author and his team are aware of the results. In the third step, I want my data to become public, because I need to contribute with these findings to the global corpus of knowledge, which might improve medical care in similar patients. Not all the truth comes for perfect randomized trials where all biases are controlled. At least some knowledge comes from everyday experience of not so perfect patients treated by not so perfect doctors and published in not so perfect journals. To publish is to make public what I have done. As we already have previously written^[8]. Latin

American research is often rejected from American or European journals without review. This leads many authors from our countries to publish in national journals, but this becomes a vicious circle, because other scientists cannot read Spanish and this knowledge does not really become public even after publication. In the fourth step, I want my findings to be noticed by others and receive views, likes or thumbs-up: citations! And I will be cited under two conditions: what I say is visible and what I say is interesting. We do not know the reasons behind the low proportion of Mexican papers published in foreign journals: did the authors decide to publish locally? Did they send the manuscript abroad and it was rejected? Did the prefer to publish it in a national journal because they think that foreign journals will not be interested? These are questions worth being asked but that nobody has dared to ask. Research must be published for others, not for the author.

Our study reveals that 2% of the studies were published in a journal with an unspecified JIF, 37% in journals with JIF of 1.00-1.99, 44% with JIF from 2.00 to 24.99 and none in journals with a high JIF (25.00-50.00). This confirms recent findings on the publications of Mexican spine surgeons [14], which shows a per capita annual index of 0.05 (one paper per author every 20 years), and that with a mean value of JIF of 0.53.

Articles are the only visible part of research, the one which precisely is *public knowledge*, because it *has been published*. Our study has three inherent weak points: 1) research that has not been published has not been considered and 2) research that is published in journals not indexed in the database are also ignored. But the situation would have been worse if we had chosen PubMed or the WoS, as the majority of Mexican medical journals are not indexed in these databases, 3) those published in minor journals were not included.

Our paper is a call for action: if we have a given proportion of patients operated at our institution, we should to transform that experience into publications. Latin American researchers should reflect on these problems present in our countries: 1) what measures could be taken to encourage publication practices? 2) How can continuous medical education programs create numerous groups of doctors with a good command of English: most of them can read, but cannot write directly in English. They often have a manuscript in Spanish with a word for translation which poorly reflects the original idea: traduttore traditore we use to say for such situations! 3) Access to first-class journals is prohibited by the pay-for-publishing policies where publications fees are not affordable and local universities have no budget for that. 4) Which other policies might improve institutional performance?

From 2000 to 2019, we have witnessed an eightfold increase in research publications, which is a significant sign of research productivity improvement in the country. The proportion of original research is important, which is an indirect proof of a certain maturity: Mexican researchers do not write review articles which is an easier task at the beginning of any scientific career. Now, we should focus on quality and impact.

Starting in the year 2000, a majority of clinical articles focused on the diagnosis and treatment of glioblastoma, the most common malignancy [15]. aggressive primary CNS Glioblastoma is one of the cancer types that require further investigation due to poor prognosis [16,17]. Our authors in molecular research on brain neoplasms have shown a preference for C6 glioma cell lines as an experimental model of glioblastoma. At the Instituto, studies with this cell line have been published primarily as a way to understand tumour growth mechanisms, as well as to test cancer therapies. International collaboration has a greater diffusion and therefore a larger number of citations. This is illustrated by this clinical paper: "Adding chloroquine to conventional glioblastoma treatment for multiforme: randomized, double-blind, placebo-controlled" by Sotelo et al., with 297 citations, and the study

on "CpG Island Hypermethylation of the DNA Repair Enzyme Methyltransferase Predicts Response to Temozolomide in Primary Gliomas" by Paz et al., with 221 citations. The first dates back to 2006 and the second to 2004. We summarize the authors on the subject in Table 3.

In the clinical field, Tena (ORCID ID: 13409398700) has authored 8% the institutional output. In the experimental domain, López (ORCID ID: 7103066402) has authored 13% of the total production, Arrieta 6% and Sotelo 5%, whereas the main corresponding authors were Pineda, Arrieta and Sotelo with 13%, 9% and 8% of the papers, respectively; Pineda and Sotelo belong to the same research group.

Conclusion.

We have few numbers of highly productive authors, but we have a positive remark. In any human group, there is an elite, but the larger the elite, the more you can count on a group revival and progress; authors (first and corresponding) published the larger number of papers (quantity) do not belong to those most cited (a surrogate marker of quality). Any young writer starts with case reports, letters to the editor, case series, but with time, more elaborated projects targeting a larger audience in more prestigious journals should be the natural evolution.

The fact that a considerable proportion of our research in this topic is restricted to national journals offers a more restricted audience for our findings. Clinical studies with more relevance would merit larger forums, and therefore we should analyze how the patterns of national and international cooperation generate publications in foreign journals. This might boost our visibility outside of Mexico and other Spanish-speaking countries. Mexican authors should participate in more international trials and projects, as the size of the country and the quality of the institutions would allow make this feasible.

With this study, we conclude that brain neoplasms research in Mexico is under

development. These findings should provide instrumental information and awareness for those who will engage in research in order to propose treatment alternatives. Along recent bibliometric analyses from Mexico [14], we agree on the fact that further strategies should be implemented to increase the number and track of Mexican contributions to the scientific literature. A national registry on brain tumors would increase our national productivity and to encourage multicentric protocols as that would raise awareness among academics from those institutions, because this gap in knowledge shows at a national level have not shown interest in this subject.

In conclusion, research on brain tumors in Mexico has recently showed buoyancy and we should profit from this inertia to give a definitive boost to it, which might benefit authors and institutional prestige. But mainly, with a more robust research, we could find better solutions for our patients, applicable in the national context.

Declarations.

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and materials: The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors contribution:

- 1. RC: Formal análisis, Validation, Writing original draft, Writing review & editing
 - 2. TM: Figures, Writing review & editing
 - 3. RD: Figures
- 4. SJ: Writing original draft, Writing review & editing.
- 5. LA: Conceptualization, Writing original draft Writing review & editing

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List of abbreviations:

Instituto Nacional de Neurología y Neurocirugía (INNN)

Instituto Nacional de Cancerología (INCAN) Universidad Autónoma Metropolitana (UAM) Gross Domestic Product (GDP)

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