RESEARCH NOTE

Research on *Babesia*: A bibliometric assessment of a neglected tick-borne parasite [version 1; peer review: 1 approved, 1 approved with reservations, 1 not approved]

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Abstract
Given the emergence and reemergence of tick-borne diseases, here we assessed the publishing patterns of research focused on *Babesia*. We also discuss the implications for the articles published in the last decade, and how more clinical and epidemiological information concerning *Babesia* is still required. The findings of this article would be useful to define research priorities about *Babesia* and diagnose the important of scientific production on this pathogen.

Keywords
Babesia, tick-borne disease, epidemiology, public health, bibliometric

This article is included in the Disease Outbreaks gateway.
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Author roles: Rodriguez-Morales AJ: Conceptualization, Data Curation, Formal Analysis, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; Bonilla-Aldana DK: Conceptualization, Data Curation, Formal Analysis, Writing – Original Draft Preparation, Writing – Review & Editing; Escalera-Antezana JP: Formal Analysis, Writing – Original Draft Preparation, Writing – Review & Editing; Alvarado-Arnez LE: Formal Analysis, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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Introduction
Babesiosis is a zoonotic disease with a global distribution; it is mainly transmitted by ticks of different genera (e.g., *Rhipicephalus* spp. and *Dermacentor* spp.) and diverse species. It is caused by infection of the erythrocytes of mammals by *Babesia* species, which are Apicomplexa protozoa of the suborder Piroplasmidea and the family Babesiidae. The vector role of ticks for these parasites was discovered by Smith and Kilbourne in 1893, who were the first to demonstrate its transmission. The first case was described by Skaraballo and occurred in 1957 in Zagreb, Croatia.

Human babesiosis is not under surveillance and notification in most countries, including those with autochthonous incidence vector-borne diseases. However, studies show that their vectors are widely distributed in tropical and subtropical areas. Research is fundamental to better comprehending this disease. The relevance of bibliometric evaluations on emerging and reemerging disease has been previously described as they can contribute in the understanding on how the global scientific and health communities respond to outbreaks. Herein, our objective was to use bibliometric approaches to analyze *Babesia* research.

Methods
A bibliometric evaluation was performed focusing on *Babesia* scientific bibliography. Six main databases were used for retrieving information: Science Citation Index Expanded (SCI-E), Scopus, Medline, LILACS, SciELO and Google Scholar. For the search pipeline we used the following combination of key words (MeSH, Medical Subject Headings): “*Babesia*” AND “Latin America”, “*Babesia*” AND “Argentina”, “*Babesia*” AND “Colombia”, and this strategy was maintained including the name of each country as a keyword. Also, “Babesiosis” was used as a substitute of *Babesia* to increase the number of results. Regarding the type of publications, we decided to include original papers, review articles, case reports and editorials, which were further stratified according to publication year and the name and institution to which the main author was affiliated at the time of publishing. This analysis included results obtained up to December 1, 2018.

Data summaries for quantitative variables (number of articles, articles per country, articles per year or periods, citations and H index) were expressed as means and interquartile ranges (IQRs), and for qualitative variables proportions are reported.

Results
Overall, 78,137 *Babesia*-associated items resulted from the initial screening of publications. From Google Scholar 62,100 articles (25% USA, 24.9% South Africa, 18.5% Japan) were recovered, followed by Scopus, with 6,272 articles (25.4% from USA, 8.5% Japan, 7.2% UK), and Medline with 5,045 articles (13.7% USA, 10.1% Japan and 5.2% China) (Table 1). From Web of Science, 4,330 publications were retrieved (28.06% from USA, 11.4% Japan and 7.37% Brazil), followed by LILACS with 202 articles (29.2% Brazil, 2.4% Mexico, 1.9% USA) and

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SciELO with 188 articles (26.6% Brazil, 3.1% Mexico) (Table 1). Considering the Medline database, the number of research articles on Babesia increased above 100 publications per year only after 2004 (Figure 1).

In the case of Scopus, the median number of articles published each year as of 1970 was only one (IQR: 0-3), from 1970 until 1995 this number increased to 64 (IQR: 56-73) and from 1996 till 2018 was 188 (IQR: 115–271) (Figure 2). At Scopus 134 countries contributed a minimum of one paper over the study period. For SCI-E, the annual median number of articles reported from 1996 until 2018 was of 99 (IQR: 96-103) (Figure 3), with at least one article published from 129 countries during the study period.

“Obihiro University” in Hokkaido, Japan, was the institution with the most productive research in Scopus, and “Igarashi, I” was the author with the largest record in Babesia research, with 210 articles (Figure 4 and Figure 5). At Web of Sciences, the H index for the topic is 88, with 70,950 citations, reaching 7,734 citations in 2017 (Figure 6).

The raw data generated in this study are available on OSP.

Discussion

The results presented here show that the USA and Japan have primary roles in Babesia research, with USA leading the scientific production with nearly quarter of the published articles, followed by Japan and the UK (Table 1). Certainly, in USA, tickborne disease occurrence is frequent especially in certain areas and months over the year. Tickborne diseases such as babesiosis are commonly reported in Northeastern states as well in the upper Midwest, often with higher incidence in summer. In addition, blood transfusions is still a matter of concern, even in the USA10–13. In countries in Asia, such as Japan, human babesiosis was not reported until fairly recently (1999), when a symptomatic case was describe in Kobe City, Hyogo Prefecture, Japan14,15; however, since then research has significantly increased in this country. Authors from UK have collaborated with research with others from endemic countries. However, in 2006 and 2016, two cases of autochthonous canine babesiosis were reported in the UK. Since November 2015, there have been at least three more cases of canine babesiosis in untraveled dogs from Essex, all were confirmed B. canis infections by PCR. Dermacentor reticulatus ticks were found on the dogs16.

One of the relevant aspects surrounding babesiosis is that there are not yet licensed human prophylactic vaccines, and treatment alternative remain limited. Two commonly used antimicrobial regimes are highly effective: the combination of atovaquone and azithromycin and the combination of clindamycin and quinine17. Thus, most preventive measures are needed to reduce the risk of infection from ticks and wild and domestic reservoirs (e.g. rats).

Bibliometric analyses contribute an objective vision of the scientific activity of a country or a region, in an investigative area. In the particular case of infectious diseases, there are different reports about its utility5–8, especially in emerging infectious
Figure 2. Research trends on *Babesia* from 1931 to 2018, Scopus.

Figure 3. Research trends on *Babesia* from 1996 to 2018, Web of Science.
Figure 4. Top research institutions that published scientific literature on *Babesia*, Scopus.

Figure 5. Top research authors that published scientific literature on *Babesia*, Scopus.

Figure 6. Citation trends on *Babesia* from 1931 to 2018, Web of Scopus.
diseases16–21, being possible to establish and to compare the amount of scientific production in journals, institutions, and authors publishing about a certain issue; this would allow establishment of a plan in terms of scientific policy as well in other matters21. No previous bibliometric studies about babesiosis or Babesia have been found in the consulted bibliographical scientific databases.

In conclusion, it is time to translate research findings into effective control of babesiosis. As occurs with other emerging diseases, research leading to vaccinal or effective therapeutic options are of utmost importance. Tick-borne pathogens such as Babesia and others with even clearer epidemic potential need to be researched more and to be prioritized with effective interventions to reduce their negative impact.

Data availability
Raw bibliometric data generated in this study are available on OSF. DOI: https://doi.org/10.17605/OSF.IO/ER9UP.

Grant information
The author(s) declared that not grants were involved in supporting this work.

References

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The manuscript submitted by Rodríguez Morales et al. represents a bibliometric evaluation on Babesia, in order to contribute to understanding this neglected zoonosis and addressing future research and control strategies. Bibliometric evaluation is an excellent tool to obtain objective information about specific areas of research and support the adoption of strategic decisions. In detail, this study provides and summaries data on the research activity on Babesia worldwide. It shows that the main country involved in the research on Babesia is USA, where babesiosis is a notifiable disease since 2011 (CDC) and most human cases have been reported. Of interest the strong research activity of institutions and countries as Japan and UK, in which Babesia represents a new emerging problem both in animals and humans. This study highlights the increased research activity on this neglected zoonosis, considered of growing importance in several countries and the need of further studies addressed to preventive and therapeutic aspects.

The manuscript, proposed as a research note, is well structured, the statistical analysis and its interpretation is sufficient, results and discussion appropriate. To fulfil F1000Research criteria ("Research note … can be reported with one or two illustrations (figures/tables)"), authors could reduce the number of figures/graphics.

I suggest the following minor revisions in the text:

In the Introduction:

- I suggest to add *Ixodes* spp as tick genera involved in the transmission of Babesia to humans. Indeed in USA most reported human cases are attributed to *B. microti* transmitted to people by *Ixodes scapularis*. Moreover, most European human cases are caused by *B. divergens* and *B. venatorum*, primarily transmitted by *Ixodes ricinus*.

- The authors should specify that the first case described in Croatia in 1957 by Skaraballo, refers to a "human" case.

- Moreover I suggest adding a sentence regarding the role of animal reservoirs and their distribution that contributes (as the presence of vectors) in the maintenance of the transmission cycle.

In the Methods:

You could clarify which and/or how many countries have been used as keyword for the search pipeline
Figure 6: In the caption: the citation trends is from Web of Science (as reported in the results), not Scopus.

References

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Diagnostics on vector borne disease, neuropathology, surveillance program

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
citation, author, institute and country.

Unfortunately the article has major deficiencies. The most obvious of these is that the human and animal versions of the disease have been conflated so that the data are more or less meaningless. The economic impact, research priorities and research constraints are very different in veterinary compared with medical babesiosis. In fact it is possible to argue that even the parasites are different, since the vast majority of human cases are caused by a parasite (*Babesia microti*) that is only distantly related to those prevalent in veterinary babesiosis (*Babesia sensu stricto*), and there are differences in their biology such as presence or absence of transovarial transmission, sensitivity to antibabesials, availability of in vitro cultures etc.

Additionally, it is difficult to see the point of counting numbers of articles published by different countries, authors, institutions etc. Cross comparison of these data is invidious since different interests and time scales are involved. Such data may tell the reader something about where there has been sufficient interest for research funding but nothing about the nature of the research, which is necessary to identify areas of neglect. It would have been much more useful to break the data down by topic. For example, how many articles are in the area of pure immunological research, usually involving rodents, how many address therapeutic issues, how many vaccination, how many epidemiology etc. Only then would it be possible to see where the gaps are, particularly in relation to practical measures, particularly if accompanied by analytical comments. The superficial approach of this article certainly does not, especially when there has been no attempt to explain the trends presented in the figures.

The authors have identified some research areas that require more attention, for example blood transfusion infection in the USA, development of vaccines (presumably molecular), development of new antibabesials, but have not provided the necessary context or evidence for these conclusions.

Some important issues that the authors seem to have ignored completely, include the development and successful use of live vaccines for cattle babesiosis over a long period of time, the prodigious, but failed efforts, to produce molecular vaccines against cattle babesiosis (which indicates the very great difficulty involved in the development of vaccines for human use), the change in direction and emphasis of babesiosis research in general with the discovery of *B. microti* in the US, and epidemiological issues such as the extension of the geographical range of infections, although briefly touched on in relation to the UK, for reasons that are not clear.

The references make little mention of established authorities in the topic and there are at least five instances of self-citation. Finally there are many examples of poor sentence construction (e.g. the last part of the last sentence in the abstract, inaccurate statements (e.g. the first sentence in the Introduction and the first sentence in the second paragraph), unnecessary sentences (e.g. the third sentence in the second paragraph) etc. There are more of all these in the Discussion.

Overall, the impression gained is that the authors have made use of readily available metrics on the internet, to present data that appear to have no useful meaning and have not attempted to analyze the data to achieve their stated objectives.

**Is the work clearly and accurately presented and does it cite the current literature?**

No

**Is the study design appropriate and is the work technically sound?**

No
Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Not applicable

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Parasitologist, with special interest in babesiosis and tick-borne diseases

I have read this submission. I believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 08 February 2019

https://doi.org/10.5256/f1000research.19225.r42304

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Stalin Vilcarromero
Sociedad Científica de Estudiantes de Medicina de la Amazonía Peruana (SOCIEMAP), Facultad de Medicina, Universidad Nacional de la Amazonía Peruana, Iquitos, Peru

In the manuscript entitled “Research on Babesia: A bibliometric assessment of a neglected tick-borne parasite” the authors try to evaluate the previous bibliometric research regarding babesiosis in the world. It has recognized the value of this type of study because it helps to identify the importance of a country, institution or researcher in solving problems based on scientific evidence. Most of them describe bibliometrics in their papers considering bibliometric variables such as number of citations, author participation in research production, author and co-authorship analysis with VOSviewer1, the H-index, geographical distribution of that disease by countries, the amount and intensity of their international collaboration, analysis of that research based on the frequency of the words used in the title of the articles 2, number of publications with intra-country collaboration, number of publications with inter-country collaboration3,4 etc, and usually, the literature was retrieved using only one database (Scopus, Medline, etc) which may give the advantage to let them analyze this in depth.

However, when the number of publications is normalized by population1, by gross domestic product, and by gross national income per capita6, health expenditure6, scientific collaboration7 or other important variable (epidemiology variables such as prevalence, incidence6, endemic versus non-endemic, etc) it makes more relevant the study. On the other hand, it is known the capacity of databases such Scopus,
Medline, Web of Science and Scielo, and the authors may decide to use only one giving more details to the analysis.

In this case, considering that Babesiosis is a neglected disease, of importance in several countries as it has been described in the manuscript, so this topic deserve still more research, so I consider that this bibliometric analysis would be important for the scientific community. However, it would also be important to normalize the number of publications (including some of those variables mentioned above), include other bibliometric variables such as H-index.

References

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes
Are the conclusions drawn adequately supported by the results? 
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical and epidemiological research in Vector Borne Disease

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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