Research trends in Carrion's disease in the last 60 years. A bibliometric assessment of Latin American scientific production

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Carrion’s disease is a major re-emerging and occupational health disease. This bibliometric study aimed to evaluate scientific production on this disease both globally and in Latin America. SCI-E, MEDLINE/Go-PubMed, SCOPUS, SciELO, and LILACS databases were searched for Carrion’s disease-related articles. They were classified according to publication year, type, city and institution of origin, international cooperation, scientific journal, impact factor, publication language, author(s), and H-index. There were 170 articles in SCI-E. The USA was the largest contributor (42.9%), followed by Peru (24.1%) and Spain (12.4%). Latin American publications were cited 811 times (regional H-index=18). There were 335 articles in SCOPUS: 25.9%, 11.6%, and 8.3% were published by the USA, Peru, and Spain, respectively. Latin American publications were cited 613 times (H-index=12): Peru, Colombia, and Brazil received the most citations (n=395, H-index=10; n=61, H-index=1; and n=54, H-index=4, respectively). The most scientifically productive American institution was the University of Montana (2.9% of American production). In Peru, it was the Institute of Tropical Medicine Alexander von Humboldt of Peruvian University Cayetano Heredia (6.5% of Peruvian scientific production). There were 3,802 articles in Medline (1.2% were Peruvian), 35 in SciELO (94.3% were from Peru), and 168 in LILACS (11% were published in 2010–2014; only one article was published in 2015). Scientific production worldwide is led by the USA, and, in Latin America, by Peru and Brazil. However, Latin American scientific production in bibliographic databases is much lower than in other regions, despite being an endemic area for Carrion’s disease.

Keywords: Carrion’s disease, Oroya fever, Verruga peruana, Bibliometric analysis, Latin America.

INTRODUCTION

Carrion’s disease is a bartonellosis also known as Oroya fever, “verruga peruana” (Peruvian warts), or “SIDA cholo” [1]. While it is an autochthonous disease of high-altitude (500-3,200 meters above sea level) valleys of the Andean Mountains in South American countries (especially Peru, Ecuador, and Colombia), numerous outbreaks have been reported in other, previously non-endemic, areas in Latin America in the last two decades. In particular, the disease has expanded into new forest areas and other regions of Peru. Moreover, in
2004, there was a major outbreak of Carrion’s disease throughout the whole of Peru that resulted in more than 11,000 cases, with a fatality rate of 0.6% [2, 3]. Consequently, Carrion’s disease is currently regarded as a re-emerging disease [4]. Carrion’s disease is caused by *Bartonella bacilliformis* and is transmitted from an infected human or carrier to a healthy one by the bite of the sandfly *Lutzomyia sp.* [5,6]. The entry mechanism has been slowly clarified for the Bartonella sp., and includes participation of pathogen’s Bartonella effector protein into hosts cells. Moreover, the bacterium infects different type of cells, including primarily erythrocytes (where it causes a long-lasting bacteremia) and also nucleated cells [7].

Classically, it consists of three clinical phases. The first is the acute hematic phase known as Oroya fever. It is characterized by fever, severe anemia, and transient immunosuppression. This phase, if the patient survives it, is followed by an intermediate phase that is usually asymptomatic. About 4 to 6 weeks after the initial infection, the third phase, the chronic eruptive phase (Peruvian warts), commences. It is characterized by the development of a chronic cutaneous rash caused by the proliferation of endothelial cells [4, 8]. It was once believed that the first and third phases corresponded to different diseases. However, this notion was dispelled in 1885 by the Peruvian medical student Daniel Alcides Carrion. Carrion hypothesized that Oroya fever and verruga peruana were different phases of the same infectious disease. While this notion was shared by many physicians at that time, it had never been formally tested. Carrion thus inoculated himself with the contents of a skin lesion from a patient with Peruvian warts. He developed the acute phase of the disease, thus proving that both diseases have the same origin. He died as a result of his remarkable act [9, 10].

Traditionally, this disease tended to occur predominantly in foreign workers who arrived in endemic areas to perform various tasks, such as the workers who were constructing the railway between Lima and La Oroya. However, nowadays, it is also increasingly being observed in people who arrive in the endemic areas from different parts of the countries and from abroad due to population movements; these include farmers, teachers, and doctors along with construction workers. This has reinforced the idea that, at present, Carrion’s disease is an occupational disease [8].

In general, very little is known about the incidence of Oroya fever and/or Peruvian warts [4]. However, in 2015, the National Epidemiology Department of the Ministry of Health of Peru issued an epidemiological bulletin showing that the cumulative incidences of Oroya fever and Peruvian warts in 2015 were 0.22 and 0.12 per 100,000 inhabitants, respectively [11]. Children appear to be particularly affected by bartonellosis outbreaks: their mortality rates borders on 10%. An estimate of the population at risk of Carrion’s disease is 1.7 million people who live in an area of 56,000 square miles [12].

The geographical expansion of Carrion’s disease and the increasing numbers of outbreaks and cases in the last two decades may reflect due to El Niño phenomenon, which may have expanded the range of the sand-fly vector [2]. Given that Carrion’s disease is now a re-emerging infectious disease, it is important to assess what is currently known about Carrion’s disease. This will help to encourage research in this area, particularly regarding the current epidemiological situation in endemic areas and how the disease can best be diagnosed, prevented, and treated. To this end, we performed a bibliometric evaluation of the scientific publications in Latin America and worldwide that focus on Carrion’s disease.

### MATERIALS AND METHODS

A bibliometric descriptive study on the global scientific research on Carrion’s disease was methodologically performed based on our previous manuscripts [13,14]. There was a particular focus on Latin America given that this disease is historically the area that has been most affected by Carrion’s disease. Thus, the following publication databases were searched: Science Citation Index-Expanded (SCI-E) supplied by Thomson Reuters (1957-2015), SCOPUS provided by Elsevier (1976-2015), Index Medicus/Medline/PubMed by GoPubMed® (1970-2015), ScIELO (1981-2014), and LILACS (1985-2014). The latter two databases focus on articles from Latin America; all are written in Spanish but some are also translated into English.
The search words were identified from Descriptors of Health Sciences (DeCS) and Medical Subject Headings (MeSH). They were “Carrion disease OR verruga peruana OR Oroya fever”. This search was performed in July 27-31, 2015. The following data were retrieved: the year of publication, number and type of scientific manuscripts, city and institution of origin, presence of international cooperation, scientific journal, impact factor of the journal, language of the publication, authors, and authors’ H-index for Carrion Disease issue. All types of studies were included. Data were tabulated and processed in Excel 2013® for Windows 7®. Quantitative variables were expressed as mean and standard deviation, while qualitative variables were expressed as number and percentage.

### RESULTS

**Science Citation Index-Expanded (SCI-E)**

In total, 170 publications matching the search words were retrieved from SCI-E. Of these, 30% ($n=51$) were published by authors from Latin American countries, 73.5% ($n=125$) were original articles, and 27.1% ($n=46$) were published in the last 5 (2011-2015) years (on average 9.2 articles per year, 3.7 Standard Deviation [SD]). The countries of origin with the most articles were the USA (42.9%, $n=73$) and Peru (24.1%, $n=41$), followed by Spain (12.4%, $n=21$), France (10%, $n=17$), and England (4.7%, $n=8$). The countries with less contributions were Chile and Ecuador (each 0.6%, $n=1$). The authors with the most published articles in the world were as follows: M.F. Minnick, who is from the USA and authored 13.7% ($n=10$) of the manuscripts published by the USA; C. Maguía, who is from Peru and authored 24.4% ($n=10$) of the articles published by Peru; N. Solorzano, who is also from Peru and authored 19.5% ($n=8$) of the Peruvian articles; and D. Raoult, who is French and authored 47.1% ($n=8$) of the articles published by France. According to the SCI-E database, the articles authored by Latin Americans were cited 811 times in total (on average, 20.3 citations per year in the last 5 years [2011-2015], 26.7 SD), thus generating an H-index of 18 for the region (Figure 1).

The journal with the highest number of publications on Carrion’s disease was the *American Journal of Tropical Medicine and Hygiene* (8.2%, $n=14$): this journal focuses on infectious diseases, parasitology, virology, and miscellaneous areas and has an impact factor of 2.699. The next most prolific publishers were *PLoS One* and the *Journal of Clinical Microbiology* (each 2.9%, $n=5$), which focus on life sciences (biochemistry, genetics, and molecular biology) and medical microbiology, respectively: their impact factors are 3.534 and 3.993, respectively. These journals were followed by the *New Zealand Veterinary Journal* and the *International Journal of Infectious Diseases* (each 2.4%, $n=4$), which focus on veterinary science and infectious diseases, respectively, and have impact factors of 1.256 and 2.33, respectively.

![Figure 1 - Number of times Latin American authors of articles on Carrion’s disease were cited in 1976-2015, according to Science Citation Index-E.](image-url)
Scopus
In total, 335 articles on Carrion’s disease were found in SCOPUS. Of these, 17.6% (n=59) were published by Latin American authors, 73.7% (n=247) were original articles, and 71 original articles (28.7% of the original papers) were published in the last 5 (2011-2015) years (on average, 5.1 original articles per year in the last 5 years, 5.7 SD). In January-July 2015, 11 new scientific articles on Carrion’s disease were published.
Authors from the USA produced 25.9% (n=87) of all scientific articles on Carrion’s disease, followed by Peru (11.6%, n=39), Spain (8.3%, n=28), France (5.9%, n=20), and Italy (3.5%, n=6). The country with less contributions was Venezuela (produced 0.3% [n=1] of the total). The numbers of scientific publications on Carrion’s disease that were ever produced by the different Latin American countries are shown in Figure 2.
In the USA, the country with the highest scientific article production, the institution that generated the most scientific articles was the University of Montana: it produced 2.9% of all articles worldwide (n=10). As a result, it was the most prolific publishing institution worldwide. The author who generated the most scientific articles was M.F. Minnick from the Division of Biological Sciences at the University of Montana. This author produced all ten of the scientific publications produced by this university. His H-index was 5.
In Peru, the institution that generated the most scientific articles on Carrion’s disease was the Institute of Tropical Medicine Alexander von Humboldt of Universidad Peruana Cayetano Heredia (UPCH): it generated 6.5% (n=3) of the scientific articles produced by Peru. The author with the most scientific articles was C. Maguña, who was affiliated at the Institute and produced 4.7% (n=16) of all publications and had an H-index of 5.
In Spain, the institution that generated the most articles on Carrion’s disease was the CSIC-Museo Nacional de Ciencias Naturales (MNCN): it produced 14.2% (n=4) of the publications generated by Spain. In France, the Faculty of Medicine at the University of Aix-Marseille produced most articles, accounting for 40% (n=8) of the French production. The University of Turin generated 16.6% (n=2) of the articles published by Italy. The authors who generated the most articles in Spain, France, and Italy were J.A. Lemus (17.8% of all Spanish articles, n=22; H-index=4), D. Raoult (35% of all French articles, n=7; H-index=5), and G. Savini (16.6% of all Italian articles, n=2; H-index=2).
The country whose publications were cited worldwide most often was Switzerland (408 citations, H-index=7), followed by France (331 citations, H-index=10). Looking at Latin America more closely (613 citations, H-index=12), papers published by Peru were cited the most often (395 times, H-index=10), followed by Colombia (61 citations, H-index=1), Brazil (54 citations, H-index=2).
The countries that produced the most scientific publications were the USA (26.9% of all publications, \(n=1021\)), France (8%, \(n=306\)), Spain (4.8%, \(n=182\)), Germany (3.2%, \(n=120\)), and Japan (2.5%, \(n=96\)).

Of the total, 4% \((n=152)\) were produced by Latin American authors, with Peru being the second prolific country \((n=47, 1.2% \text{ of all publications})\) behind Brazil \((n=48, 1.2% \text{ of all publications})\). Of the 47 articles published by Peru, 19.1% involved international cooperation. Moreover, in this country, the author who published articles on Carrion’s disease most frequently was C. Maguiña, who produced 14.9% \((n=7)\) of all Peruvian publications, as indicated by the collaborative network map shown in Figure 4.

In the USA, the author with most contributions was E. Breitschwerdt (5.6% of all American articles, \(n=57\)). In France, D. Raoult was the most prolific author (40.8% of all French publications, \(n=125\)), while, in Spain, Germany, and Japan, the most productive authors were J. Carrion (4.4%, \(n=8\)), A. Sander (10%, \(n=12\)), and M. Tsukahara (18.8%, \(n=18\)), respectively.

The journals that published most articles on Carrion’s disease were as follows: the *Journal of Clinical Microbiology* (3.8%, \(n=144\) of all publications), which publishes laboratory studies on human and animal infections and has an impact factor of 3.993; the *Emerging Infectious Diseases*
Carrion’s disease in Latin America

Journal (2.1%, n=79), which targets emerging and re-emerging infectious diseases and has an impact factor of 6.5; Clinical Infectious Diseases (also 2.1%, n=79), which focuses on infectious diseases and has an impact factor of 8.886; the American Journal of Tropical Medicine and Hygiene (1.5%, n=56), which focuses on tropical medicine and has an impact factor of 2.699; and the Pediatric Infectious Disease Journal (1.4%, n=55), which targets infectious diseases in children and has an impact factor of 2.723.

SciELO
In total, 35 articles were found in the SciELO database, which only contains Latin American publications. Of these, 34.3% (n=12) were published in the last 5 years (2010-2014). None were published in 2015. The only countries that contributed were Peru (94.3%) and Brazil (5.7%). The scientific journals in which these articles were reported were Acta Médica Peruana (42.9%) and Revista Peruana de Medicina Experimental y Salud Pública (37.1%). Only one (2.7%) of the articles found in SciELO was published in English.

LILACS
In total, 168 articles were found in the LILACS database, which also only contains Latin American publications. Of these, 11% were published between 2010 and 2014. Only one article was published in 2015. Only 22 (12.8%) of the articles found in LILACS were published in English.

DISCUSSION
The objective of this bibliometric study was to evaluate the amount and quality of scientific publications on Carrion’s disease in Latin America and worldwide. This type of study is useful for directing research efforts and improving fruitful collaboration, both regionally and globally. Bibliometric studies have been performed on other vector-borne infectious diseases such as malaria, leishmaniasis, and dengue even in parasitic zoonosis like paragonimiasis, but not yet on Carrion’s disease. However, in 2012, Sánchez Clemente et al. performed a systematic review on Carrion’s disease, while, in 2013, Prutsky et al. reported their systematic review and meta-analysis on this disease; both studies browsed databases similar to the ones assessed in our study [14,15,18-20]. Their respective aims were to help guide the research agenda for elimination of the disease and to summarize the evidence regarding the treatment of Carrion’s disease that is caused by Bartonella bacilliformis which is one of the three most common species of the genus Bartonella in humans, along with B. henselae and B. quintana [19, 20]. However, in both studies, very few articles were recovered and those that were retrieved were found to have a low level of evidence. As a result, Prutsky et al. suggested that more clinical trials are needed to identify the most optimal treatment for Carrion’s disease [20]. Likewise, it has been suggested that adequate research focused on diagnosis and sur-
veillance systems could increase visibility and contribute with eradication strategies [21].

According to the databases analyzed in this article, the scientific production on Carrion’s disease worldwide is led by the USA, which generates nearly half of all global production (42.9%). This is despite the fact this country is not an endemic area for the disease. This can be explained by the high level of American scientific production in all areas (SCOPUS ranks the USA as the most scientifically productive country worldwide), contributing with over fourth of the worldwide high impact scientific production. According to SCI-E, SCOPUS, and GoPubMed, European countries, namely, Spain and France, also contributed prominently to publications about this disease. As a result, they were ranked as the third and fourth most productive countries in terms of Carrion’s disease-related publications in the world, respectively [22].

According to SCOPUS, the Latin American countries that most frequently published on Carrion’s disease were Peru (11.6% of all publications) and Brazil (2.3%). However, according to GoPubMed, which is the database that generated the most retrieved articles, Brazil is the leader in scientific publications on Carrion’s disease; Peru produced one publication less than Brazil. The difference between these countries is that Brazil, in general, has the most intense collaborations in South America and is the most scientific productive in Latin America, contributing with 2.8%; compared with the <0.1% from Peru [1, 2]. The next most prolific Latin American countries were Mexico (2%), Ecuador (0.9%), and Colombia (0.6%). This disparity between Latin American countries may relate to the differing incidences of the disease in these countries: the countries with the highest production also tended to be those with the highest prevalence or their international collaboration provided (23).

This is supported by the fact that particularly low producers of scientific publications on Carrion’s disease in Latin America were Argentina and Venezuela, where the prevalence of the disease is zero.

On the other hand, endemic countries like Ecuador do not have a scientific production according to their prevalence, this is supported by the fact that Carrion’s disease is not reported by the Ministry of Health of Ecuador as a notifiable disease but in Peru it is reported monthly in the epidemiological surveillance system [24, 25].

In Peru, the high scientific production may reflect the fact that the country’s borders include the Peruvian Andean mountain range, which is considered to be an endemic area (24-26). Moreover, the strong increase in Peruvian scientific production since 2012 (22 articles were published between 2012 and 2015, as shown by SCOPUS) may be due to the fact that the burden of Carrion’s disease rose markedly in Peru, starting in 2010. As a result, in 2014, the cumulative incidence was 1.9 per 100,000 and the case fatality rate was 1.3% [3, 29].

The institution in Peru with the highest number of publications on Carrion’s disease was the Institute of Tropical Medicine Alexander von Humboldt of the UPCH. According to SCOPUS, this institution is the most scientifically productive institute in the world in terms of Carrion’s disease. This largely reflects the high publication rate of the Peruvian author C. Maguña, who, according to SCOPUS, was the most scientifically productive author in the world regarding Carrion’s disease. This can be explained by the nearly 30 years of research dedicated to this disease, and by the multiple international collaboration [30].

The relative research interest worldwide was highest in 1993-2003. This may reflect the fact that the registration of Carrion’s disease cases in Peru started rising in 2002 before peaking in 2004 [31].

In SCI-E, SCOPUS, and PubMed, the Journal of Clinical Microbiology, the American Journal of Tropical Medicine and Hygiene, and PLoS One tended to be in the top five most scientifically productive journals. However, only one of the Latin American journals, namely, Revista Peruana de Medicina Experimental y Salud Pública, was classed as an important journal for Carrion’s disease publications.

In SCOPUS (but not the other databases), this journal was found to be the third most productive journal in the world. Given that Latin American countries are significant contributors of Carrion’s disease publications, the fact that Latin American authors tend to favor non-local journals may reflect the possibility that local authors seek greater visibility by publishing in foreign journals [32].

The Latin American database SciELO found that only two journals, Acta Médica Peruana and Revista Peruana de Medicina Experimental y Salud Pública, published articles on Carrion’s disease (42.9% and 37.1%, respectively). However, only the latter journal was reported by SCOPUS to be an important publication for articles on Carrion’s disease.
This phenomenon has also been observed regarding scientific production in other biomedical topics [33].

Among the limitations of this study is that its results cannot be directly compared with those of other bibliometric studies on this subject because such studies have not been performed. Moreover, there is no uniformity between the different databases in terms of the variables that were reported because some of the indicators were only reported by specific databases. Nevertheless, the present study is useful as it serves as a starting point for further research.

In conclusion, worldwide scientific production in relation to Carrion’s disease is led by the USA, and, in Latin America, by Peru and Brazil. However, Latin American scientific production in bibliographic databases is much lower compared to the bibliographic production of other regions, despite Latin America being an endemic area.

Conflicts of interest
Dr. Culquichicon’s work is sponsored by the training grant D43 TW007393 awarded by the Fogarty International Center of the US National Institutes of Health. The rest of the authors declare there is no conflict of interest.

REFERENCES


