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Two decades of research on tuberculosis in Brazil: state of the art of scientific publications

ABSTRACT

The trends of scientific articles about tuberculosis in Brazil published between 1986 and 2006 were analyzed. This analysis included Capes database-indexed dissertations and theses and papers indexed in Medline and SciELO. Papers containing the word "tuberculosis" and authors affiliated to Brazilian institutions were included in the assessment. The analysis showed initially case report and review publications, and later it shifted to original articles on science, technology and innovation. These changes may reflect the strengthening of scientific research activities and new attitudes regarding tuberculosis research objectives in academic institutions in recent years. Although many theses used qualitative methodology, few qualitative publications were found, possibly because of the quantitative orientation of many journals. Qualitative versus quantitative research and education versus research-oriented publications are discussed, together with public policies and strategies to include research as a tool to control diseases. The use of the same methodology is suggested to assess the trends in research on other neglected diseases.

KEY WORDS: Tuberculosis. Academic dissertations [Publication Type]. Research, trends. Qualitative research. Publications for science diffusion. Education, Public health professional.

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INTRODUCTION

Tuberculosis (TB) remains, even in this millennium, the leading killer infectious disease in the world, with 1.6 million deaths in 2005. One third of the world population is infected by *Mycobacterium tuberculosis* and a great proportion of the population may develop and transmit the disease to the community.[5] There is no efficient vaccine against TB yet, and the diagnosis still depends on sputum examination which has only 60% to 70% sensitivity. The long time requested for mycobacterial growth, and the current treatments for the disease and the infection are unsatisfactory because they are long and may present adverse effects in different populations, hindering its management.

After an initial euphoria in the 1970's and 1980's, high cure rates were seen with the short anti-TB regimen using isoniazid and rifampin in phase III (efficacy) clinical trials. This led to the belief that TB was under control, leading to a reduction in the interest of scholars, and the civil society in tuberculosis.

In parallel, a decrease in the political commitment of managers and in the quality of TB control actions was observed worldwide. These actions were characterized by low cure rates (60% to 70%) with the short regimen used in routine situations (pragmatic trials – phase IV), increase in treatment default associated with the appearance of multiresistant strains (resistant to isoniazid

and rifampicin, MDR), and with extensive resistance (resistant to all first line drugs, XDR).[1,2]

Additionally, impoverishment, urbanization, growth of shanty towns, and the HIV pandemics in big cities increased TB incidence, even in developed countries, where it seemed to be under control, as of the beginning of the 90's in the 20th century. To fight this situation, the World Health Organization[4] (WHO) declared TB in 1993 as a global emergency and proposed the Directly Observed Treatment Strategy (DOTS) to increase detection and cure rates.

Despite the reduction of treatment default rates and of TB incidence in countries with low HIV prevalence, where the DOTS strategy was introduced, TB remained pandemic. In 2006, a new worldwide plan to control TB proposed by WHO was published: the Stop TB Partnership.[3] In this new plan, among other strategies, the conduction of the following researches was considered as a priority: epidemiology, mathematic models, applied basic research, clinical research (explanatory and pragmatic clinical trials) for new diagnostic methods, drugs and vaccines, operational research, and surveys in health systems (cost-effectiveness studies, clinical importance) in Health Units (primary, secondary and tertiary care) and in the activities of the control program, with the effective participation of representatives of the civil society.

Brazil is one of the 22 countries which present 80% of TB cases in the world.[1] Important innovative actions for health assistance have been implemented[5] in the country by the National Health System (SUS), enabling the National Control Tuberculosis Program (PNCT) to decentralize its actions to primary care services. However, the encouragement in health research did not follow this trend. In the 80's and 90's, teaching/researching institutions and health institutions were apart, because there was no clear policy to foster health research. Researches were directly ordered by the managers in the Ministry of Health (MS), with no involvement of the Ministry of Science and Technology (MCT), and the Ministry of Education (MEC).

Fostering TB research in the country in that period faced these difficulties. However, as of the end of the 90's, through the strategy of Finep (Financial Agency for Studies and Projects), of the MCT, in 1996 the *Programa de Química Fina Qtrop-Tb* (Fine Chemistry Program) was launched. In 2001, the MCT started to sponsor researches in all areas of knowledge, creating the Brazilian TB Research Network (Rede TB). In 2004, with the 2nd National Conference on Health Science, Technology, and Innovation, the investment in production of scientific knowledge on neglected diseases was considered strategic for the country, including TB among them. The MS, through its *Departamento de Ciência e Tecnologia* (Decit – Science

and Technology Department) created the *Conselho de Ciência, Tecnologia e Inovação em Saúde* (Council for Science, Technology, and Health Innovation), starting the Technical Cooperation between the MS and the MCT. In that period, there was a substantial increase in the amount of financial resources for neglected diseases, such as TB.

The present study aimed at describing the state of the art of scientific publications in TB performed in Brazil in the last two decades and their correlations with policies to encourage research in the area, in the country.

METHODS

Database surveyed were: Medline, ScieELO (Scientific Electronic Library Online*)* and the theses and dissertations database at Coordination for the Improvement of Higher Education Personnel (Capes) from MEC. Indexed publications at Medline, even if on National journals, have been considered international. Surveys included articles, master theses, and doctorate theses recorded between 1/1/1986 and 11/17/2006.

The following strategies have been used:

Medline: terms used for searching were *tuberculosis AND (Brazil[ad] OR Brasil[ad])*, to find papers of authors belonging to Brazilian institutions that presented the term *tuberculosis* in any field. Searching limits used were: *subset Medline* and references in English and Portuguese.

SciELO: in advanced search, year by year was researched, using the term *tuberculosis* in all fields *(AND) Brazil, Brasil*, in the field *affiliation country, country*. Selection of articles has been manually performed and the articles that mentioned tuberculosis without the disease as a focus, such as manifestations of Aids, findings of necropsies, other mycobacterioses, tuberculosis and other mycobacteria in animals have been excluded. Duplicate articles have also been excluded.

Capes/MEC: the search was conducted in Advanced BDTD through the word tuberculosis and by the levels of theses: master and doctorate.

Articles have been classified according to type: review, original article, case report, opinion, letter, and editorial. Studies that used qualitative variables have also been recorded. Original articles, dissertations and theses have been classified according the model of study as follows:

• Clinical-epidemiological:
  – Descriptive
  – Descriptive/analytical:
    ▪ Experimental (explanatory or pragmatic clinical trial)

- ▪ Observational (cross-sectional, cohort or case-control)
  - – Ecological
  - – Interpretative-synthesis
- • Operational
- • Basic
  - – Basic (essential)
  - – Strategic (applied basic)
  - – Technological development (fields with new vaccines, new drugs, immunology, molecular biology, molecular typing, immune-serology and microbiology)
- • Mathematic models

RESULTS

At Medline, 529 articles have been found. Adding the term tuberculosis ("tuberculose OR tuberculosis") did not add any paper. After exclusion of articles that were not relevant to the study, 388 papers remained and were considered as Brazilian publications on tuberculosis on international journals. Among these papers, 219 (56.4%) have been published by authors who are members of *Rede TB*. At SciELO, 227 papers have been found, eight of which have been excluded because they were not about tuberculosis, and 62 because they were duplicates. One hundred fifty-seven articles remained, 61 of which (38.9%) were by authors who are members of *Rede TB*. In the dissertations and theses database from Capes, only dissertations and theses up to 2004 were available. There were 372 master dissertation (75 of which, or 20.2% made by authors or councilors of *Rede TB*), and 127 doctorate theses (49 of which, or 38.6% of *Rede TB*).

Figure 1 shows the evolvement of the number of the several types of publications in the period.

Figure 2 represents the amount of articles, with predominance of original articles compared to review and case reports in the period. In the Table, publications can be observed regarding the study model. Regarding type of article, 470 were original articles, 78 were review or interpretative synthesis, and 90 were case report(s).

Approach of these studies was qualitative or quantiqualitative in two of the 388 (<1%) indexed articles at Medline, in two of the 157 (1.3%) indexed articles at SciELO, in 22 of the 372 (5.9%) dissertations, and in 11 of the 137 (8%) theses.

DISCUSSION

The present study enabled to confirm that scientific production on TB in the country increased in amount and probably in quality, due to the greater number of publications in journals with peer review and quality, especially as of 2000. Publications on international journals, in particular, had a first increase in 1995, with more than ten articles per year, and a second increase in 2000, with more than 30 articles per year. The increase in publications on journals was followed by an increase in dissertations and theses, and this increase is expected to be maintained, with the inclusion on indexers of publications from 2006 last trimester, which were not part of the database when the study was conducted.

The quality of publications, judged by the type of article, has also increased. In the 1980's and the first half of the 1990's they were essentially for educational/training purposes, with predominance of review and opinions articles. Papers reported cases or small
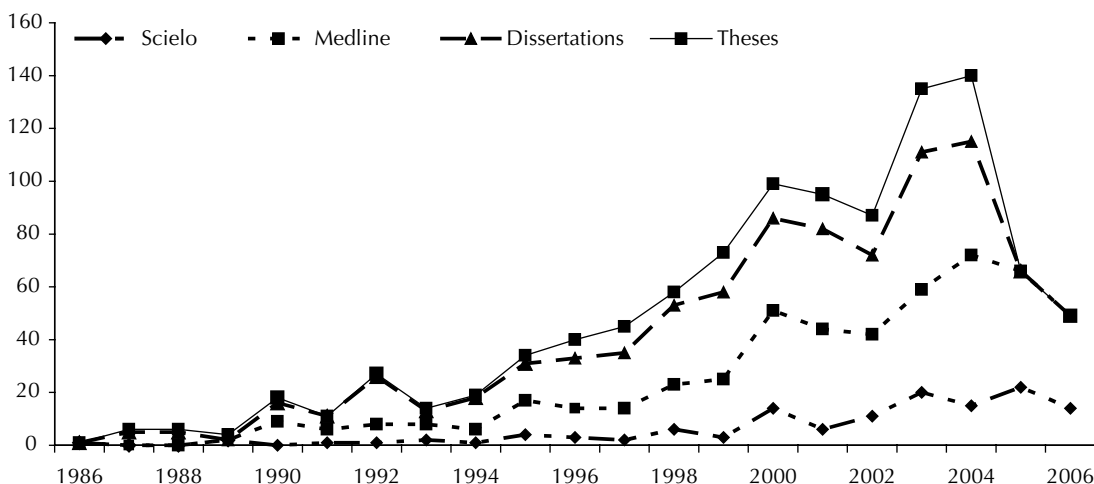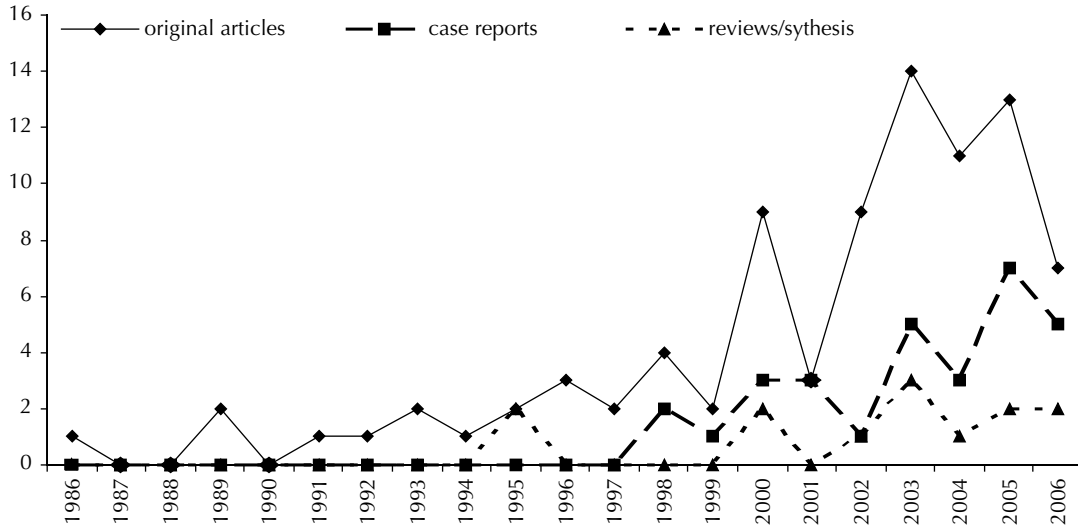

*Information on theses and dissertations in 2005 not available in 2005, and in 2006 only data on three quarters are available.
Source: Medline, SciELO, Capes thesis database, November 2006

Figure 1. Number of publications on tuberculosis by authors from Brazilian institutions, according to year. 1986-2006.*

series of cases. Although descriptive studies with small casuistic are still great part of the national publications, when publications were assessed, it was possible to observe an increase in collaborative research projects among university institutions and the health system. This boost in the amount of publications may reflect the encouragements by the MS, the MEC, and the MCT, the interest of the country's education and research

*Information on theses and dissertations in 2005 not available, and in 2006 only data for three quarters are available.
Source: Medline, SciELO, Capes thesis database, November 2006

Figure 2. Distribution of publications on tuberculosis in Brazilian institutions, according to publication year. 1986-2006.*

Table. Distribution of publications on tuberculosis of authors belonging to Brazilian institutions according to study type and methodological approach. Brazil, 1986 to 2006.

Type of article/ Methodological approach	Medline		SciELO*		Capes			
					Dissertations		Theses	
	N	%	N	%	N	%	N	%
Original articles								
Descriptive	83	21.4	46	29.3	162	43.5	27	19.7
Cross-sectional	17	4.4	14	8.9	19	5.1	8	5.8
Case-control	14	3.6	9	5.7	17	4.6	4	2.9
Cohort	13	3.4	10	6.4	15	4	8	5.8
Experimental	8	2.1	3	2	10	2.7	5	3.6
Operational	10	2.6	4	2.5	19	5.1	11	8
Basic	74	19.1	7	4.5	38	10.2	22	16.1
Strategic	75	19.3	11	7.3	60	16.1	31	22.6
Math model	5	1.3	4	2.5	4	1.1	2	1.5
Ecological	6	1.5	6	3.8	1	0.3	0	0
Interpretive-synthesis	5	1.3	4	2.5	10	2.7	10	7.3
Subtotal (original articles)	310	79.9	118	75.2	355	95.2	128	95.5
Review	28	7.2	9	5.7	9	2.4	3	2.2
Case report(s)	50	12.9	30	19.1	9	2.4	1	0.7
Technological development	0	0	0	0	0	0	2	1.5
Total	388	100	157	100	373	100	134	100

*Those already at Medline have been excluded
Capes: Coordination for the Improvement of Higher Education Personnel

institutions, and the creation of *Rede TB*. Regarding the object of publications, there is clear predominance of basic research areas with studies on vaccines, immunology, mycobacteria genetics, molecular biology, and drugs. In the operational and epidemiologic research area, studies on diagnoses and risk of the disease in vulnerable groups are predominant. This increase in publications of certain areas may be due to the priority on scientific production defined by the Post Graduation Program of Capes. The small participation of the private sector is clear, because intervention studies such as explanatory clinical trials (phase I, II, III) are rare, and they are needed to registry the products in the National System on Sanitary Surveillance (Anvisa). Noteworthy is the absence of pragmatic clinical trials that should be performed in conditions of clinical routine (phase IV), either for cost-effectiveness analysis or clinical importance of the use of new products (drugs, vaccines, diagnostic tests) and/or of new interventions in TB control actions. Such trials should be performed with the involvement of health managers, representatives of education and research institutions, and with social control. It is also important to point out the lack of technological production and of patents by Brazilian researchers, of studies on the costs related to TB control actions, on education about TB in Brazilian institutions, and the assessment of the participation of the civil society in TB control actions in the two assessed decades. In this sense, it is worth to remember the relevance of forming a network of researchers (*Rede TB*) for the synergy and communication among its members, which resulted in the publicatin of half the scientific production on journals of international circulation.

Regarding the studies methodology, predominance of quantitative studies was observed. To understand some important aspects of TB epidemics it would be necessary to perform qualitative studies, such as the access to and the quality of health services, satisfaction of health professionals and of the users of the SUS, the attitudes and beliefs of patients and relatives that lead to treatment default and mortality. When publication of theses and dissertations are compared, it is possible to observe that although some productions have used qualitative methodology, few of them were published on indexed journals.

Finally, it is suggested that the method used in the present study is employed to assess scientific production in other neglected diseases, to help defining research priorities and launching new bills.

In conclusion, although there has been a clear increase in the quantity and quality of publications after the encouragements in TB research mentioned, time elapsed is still short to notice the outcomes of this investment as knowledge production. It is recommended that the next bills to foster research by MCT, MS, and MEC have the specific objective to cover poorly explored areas in the country. As an example we mention: research in education, DOTS, costs and management, explanatory and pragmatic clinical trials, new vaccines and new interventions in TB control actions.

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