



Effect of a change in treatment time on leprosy epidemiology in Juiz de Fora, Brazil

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ABSTRACT

The impact of the reduction of treatment time for leprosy in Juiz de Fora, Brazil, from 1996 to 2004, was evaluated by examining 324 patients records. Although the time of treatment for multibacillary patients changed from 24 to 12 months, the prevalence of leprosy remained stable (~3 patients/10000 inhabitants). The incidence rate varied from 5.5 in period I (1996-1999) to 4.8 in period II (2000-2004). In both periods the multibacillary forms predominated, there being a slight reduction in cure rate (83 % to 79 %) and an increase in abandonment (6% to 11%). Interestingly, leprosy was more frequent in men in period I (62.2%), and it predominated in women in period II (55.6%), when the detection of new cases from health counseling was greater. The change in the time of treatment did not significantly alter the prevalence or incidence of leprosy which did, however, show new characteristics in the city.

Keywords: Leprosy. Leprosy /epidemiology. Treatment. Prevalence. Incidence.

1 INTRODUCTION

Leprosy is a chronic disease known for thousands of years and endemic in various developing countries. However, today scientific knowledge still is not complete as to all the factors involved in its natural history (BELGAUMKAR et al., 2007; CUNHA et al., 2007). The disease is caused by an acid-fast bacillus, the *Mycobacterium leprae*, an obligate intracellular microorganism, of slow growth, which invades mainly macrophages and Schwann cells in nerves. The dissemination of the disease in the community is related to the proportion of sensitive individuals in the population, to the opportunity for contact with infected people and to the gravity of the infection. In the great majority of individuals infected the cellular immunity of the host is efficient in combating the bacilli and the individual presents a subclinical infection. The progression of the disease in sensitive individuals follows after a long

period of incubation, which generally lasts around two to five years (BAKKER et al., 2006).

According to the Madrid classification, two stable and opposite poles of leprosy are considered: the tuberculoid (T) and the lepromatous (L) and there are two clinical intermediary forms, the indeterminate form (I) and the borderline (B) or dimorphous (D) form. In the T form, quite delimited lesions are found, anesthetic and of asymmetrical distribution. The L form is characterized by the progressive and diffuse infiltration from the skin, mucous membranes, upper respiratory tract, eyes, testicles, and nerves, among others. In the D form, lesions are numerous and the morphology mixes aspects of L and T leprosy (ARAÚJO, 2003). The I form is paucibacillary, and such like the T form can evolve naturally to cure or into another clinical form.

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Leprosy constitutes an important problem of public health in Brazil and in various countries of the world. The global number of cases in 2007 was 224717 cases (WORLD HEALTH ORGANIZATION, 2007). In spite of a global reduction taking place in the number of new detected cases, it must be considered that this reduction has been due principally to administrative actions rather than as a result of a real decline of the incidence of the disease. With the introduction of polychemotherapy, the patients who previously had a long treatment time and who had stayed on the active register for some years after having completed the treatment, were from that time removed from the active register at the end of the treatment, which today can be completed in 6 months (paucibacillary patients) or 12 months (multibacillary patients). In spite of the rate of annual case detection to be declining in the world, in America there is still an increase in this rate due to the greater detection of cases observed in Brazil (WORLD HEALTH ORGANIZATION, 2007).

In 1991, the World Health Organization (WHO) and its member states established the proposal of eliminating leprosy as a public health problem by the year of 2000, which means less than 1 case for each 10000 people. Only four countries of the 122 where leprosy was considered endemic in 1985 failed to reach this mark, among them Brazil, which occupies 2nd place in absolute number of cases in the world-wide ranking. The prevalence of leprosy in Brazil at the beginning of 2007 was 60567 and the number of new detected cases was 44436 (WORLD HEALTH ORGANIZATION, 2007).

Juiz de Fora is a city with 517029 inhabitants (population estimate for 2007) being a referral point for leprosy treatment for several nearby cities, including a region of around 762693 inhabitants (IBGE, 2002). In 1987, in this city, polychemotherapy was introduced in the treatment of leprosy, in which a combination of dapsone, clofazimine and rifampicin is used. This intervention in the assistance service made possible the reduction in the time for treating patients with the multibacillary forms from 5 to 2 years and for patients with paucibacillary form, from 2 years to 6 months. A second intervention took place in 1999, when updated technical standards recommended a greater reduction of the treatment of multibacillary patients, to a scheme of 12 doses. These standards were formalized by regulation N° 1073 of September 26th 2000 (BRASIL, 2000). Even though 2 years is the current scheme of polychemotherapy promoted by the WHO, there is no consensus among the specialists on a criterion of time in which an individual could be considered as cured (MATOS et al., 1999).

The objective of this work was to investigate the characteristics of Leprosy in Juiz de Fora in the period from

1996 to 2004, evaluating the impact of the new scheme of Leprosy treatment, introduced in 1999.

2 MATERIAL AND METHODS

This is a retrospective study of a population base using as base a total of 324 patient records from the two public treatment centres for leprosy in Juiz de Fora: the University Hospital and the Institute of Specialized Clinics of the city of Juiz de Fora. The cases of new patients diagnosed between 1996 and 2004 were selected. This interval of time was divided into two periods, period I from 1996 to 1999 (151 records) and period II, from 2000 to 2004 (173 records), based on the change of the treatment time for multibacillary patients, from 24 to 12 months, taking place in 1999.

The criterion used in period I for the patient to be considered as cured of the disease was to have completed his minimum recommended doses and not to present clinical activity of the disease (BRASIL, 1994). The criterion of cure in period II is for paucibacillary patients to complete 6 doses of supervised polychemotherapy within 9 months, independently of the number of consecutive failures, and for multibacillary patients to complete 12 doses of supervised polychemotherapy within up to 18 months, independently of the number of consecutive failures.

The clinical forms of leprosy were reported in accordance with the Madrid classification, adopted in Brazil by the Ministry of Health. The operational classification by the Ministry of Health of paucibacillary (PB) cases is used also, with up to five lesions from skin, and multibacillary (MB) cases with more than five lesions from skin (BRASIL, 2002). Sensory loss can be localized to the lesions but also thickened nerves, and the presence of acid-fast bacilli in slit skin smears. The positive bacilloscopy classifies the case as MB independent of the number of lesions using the method of Ziehl – Neelsen (ARAÚJO, 2003).

The data were analyzed using the program SPSS version 13. The analyses were done by the χ^2 test for the categorical data and with the statistical test of Kruskal Wallis for numerical data. The level of $\alpha = 0.05$ was used as criterion to find the significant differences observed.

3 RESULTS

Table 1 summarizes the principal data relative to the detection rates of new cases, prevalence and ratio of prevalence to incidence. In spite of the change in the duration of the treatment, the prevalence has remained stable varying from 2.86 in 2003 to 3.34 in 1998. The average of the prevalence was three in both periods. A peak occurred in the number of new cases detected in 1997 (7.59) followed by a fall of this value in 1998

(4.69) and a tendency of stabilization of this rate, up to the year of 2003, when it suffered a new increase (6.40). The average of the incidence in period I was 5.5 and it fell to 4.8 in period II. The ratio of prevalent cases to new cases can be considered an approximation of the time of permanence of the

patients on the active register, making evaluation of the treatment possible (ANDRADE; SABROZA; ALBUQUERQUE, 1996). Due to the stabilization of the rates that compose this indicator, the ratio also remained stable along the studied period.

TABLE 1

Number of admissions and releases from the leprosy register in Juiz de Fora in the two periods

Year	Cases ^a	Admissions ^b	Releases ^c	Population ^d	Incidence ^e	Prevalence ^f	Ratio ^g
1996	215	28	43	659695	4,25	3,25	9,28
1997	200	51	23	671.287	7,60	3,00	9,98
1998	228	32	37	680.987	4,70	3,35	8,76
1999	223	37	43	690.813	5,35	3,20	8,96
Total		148	146				
2000	217	38	34	693.611	5,50	3,10	9,21
2001	221	33	42	703.095	4,70	3,15	9,05
2002	212	37	43	710.680	5,20	3,00	9,44
2003	206	46	40	718.620	6,40	2,90	9,72
2004	212	22	34	726.542	3,00	2,90	9,45
Total		176	193				

a - number of cases of leprosy in the active register at the end of the previous year.

b - number of new cases registered.

c - number of new cases excluded from the active register due to cure, death, desertion and transfer of residence.

d - population estimate for the year.

e - incidence per 100000 inhabitants.

f - prevalence per 10000 inhabitants.

g - ratio of prevalent cases over new cases.

Font: The authors (2010).

Analyzing period I and II in reference to the percentage of cure and of abandonment for the multibacillary patients, the group in which there was a reduction of the duration of treatment, a

reduction occurred in the rate of cure and an increase in the rate of abandonment, but this difference was not significant (Table 2).

TABLE 2

Departures from the active leprosy register in Juiz de fora by period and clinical form

	Releases ^a	Períod I	Períod II	Total
Multibacillary	cure	105 ^b (82,7% ^c)	112 (79 %)	217 (81 %)
	death	4 (3 %)	3 (2 %)	7 (3 %)
	desertion	7 (6 %)	16 (11 %)	23 (9 %)
	transfer	11 (9%)	10 (7%)	21 (8%)
	Total	127 (100%)	141 (100%)	268 (100%)
Paucibacillary	cure	18 (95%)	22 (82%)	40 (87%)
	desertion	1 (5 %)	3 (11 %)	4 (9 %)
	transfer	0 (0%)	2 (7%)	2 (4%)
	Total	19 (100%)	27 (100%)	46 (100%)

a - type of exit from the active register

b - number of patients in the period.

c - percentage of patients in the period.

Font: The authors (2010).

The Graph 1 analyses the form of detection of new cases, comparing periods I and II. In both periods, referral was the most frequent way, there being a percentage increase from period I (60.3 %) to period II (71.7 %) for this data. There was a reduction in period II of the form in which the patient himself looks for health service (of 29.1 % in period I to 16.8 % in period II) as well as of the identification of cases by examination of contacts of the patients (7.9 % in period I for 2.9 % in period II). The proportion of cases in which the strategy of identification was not recorded increased from 2.6 % to 8.7 % in period II.

There was no statistically significant difference between period I and II for the clinically identified forms (Graph 2). In both periods the multibacillary forms, in other words, D and L (I - 87 % II - 84.1 %) (Table 3) predominated. The distribution of the clinical forms observed was: tuberculoid (8.0 %), indeterminate (6.4 %), dimorphic (63.1 %) and lepromatous (22.4 %). The indeterminate form was the least frequent in both periods, in spite of an increase from 5.4 % to 7.4 % which had taken place from period I to II, respectively.

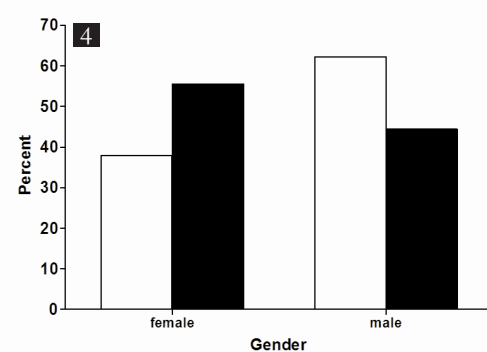
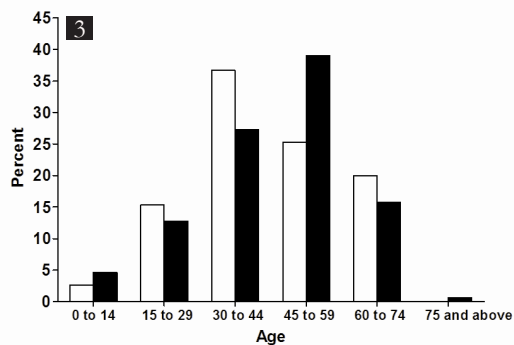
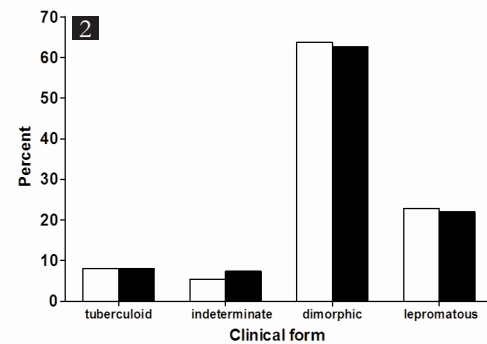
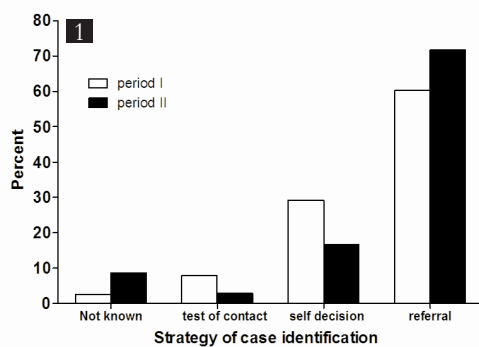
TABLE 3

Distribution of the cases of leprosy according to operational classification

	Period I	Period II	Total
multibacillary	127 (87 %)	143 (84 %)	270 (85 %)
paucibacillary	19 (13 %)	27 (16 %)	46 (15 %)
Total	146 (100%)	170 (100%)	316 (100%)

Font: The authors (2010).

In period I the most frequent age group at the occasion of diagnosis was between 30 and 44 years (36.7 %), whereas in period II the range from 45 to 59 years predominated (39.0 %). The proportion of individuals below 15 years of age in the total of new cases detected in this study was 3.7 %, not having any difference between the two periods (Graph 3). It can be seen that in period I leprosy was more frequent in the men (62.2 %) than in the women in Juiz de Fora. The women's proportion increased significantly for period II (55.6 %) (Graph 4).



Graphs 1 a 4: Characteristics of leprosy in Juiz de Fora, Brazil. In the period I (1996 to 1999) medical charts of 151 patients were analyzed, and 173 records were analyzed in period II (2000 to 2004). The form of detection of new cases (1), the distribution of leprosy according to clinical form (2), the distribution according to age group (3), and the distribution according to gender (4) were determined.

4 DISCUSSION

In this work we were interested in examining what effects may have occurred as a result of a significant change in treatment time of leprosy multibacillary patients in Juiz de Fora, Brazil. The increase of the detection of new cases of leprosy in Juiz de Fora in 1997 followed by the reduction in 1998 was similar to what was observed in the city of São Luís, in Maranhão, Brazil, in the same period. In 1998, there was also the reduction of this rate at the national level, after a period of annual growth from 1995. The fall of this indicator took place concomitant to the period when the states changed the individual notification forms used for the System of Information on Incident Notification. So, it is possible that problems in the information systems justify the observed variation (FIGUEIREDO; SILVA, 2003).

Among the measures to reach the goal of elimination of leprosy as a public health problem, the National Health Service advocates the decentralization of actions for control of leprosy. Nevertheless, in Juiz de Fora, the service is still centralized due to technical difficulties in training professionals. That might justify the high rate of abandonment in the patients studied, since accessibility is essential for integral attention to these individuals. Regarding the percentage of cure of the patients, the results suggest that the reduction in the number of doses administered to the multibacillary patients did not reduce the efficiency of the treatment for this group. Cure rates near 80 % have been maintained, similar to those observed in a study carried out in Duque de Caxias, in Rio de Janeiro from 1990 to 2003.

The increase in the frequency of patients sent for treatment of leprosy in period II suggests a greater capacity of the services for diagnosing and referring patients for treatment, which can be connected with the extension of coverage of basic service through the family health program, which has the leprosy control program as a strategic action (BRASIL, 2002). The reduction of the cases diagnosed from spontaneous presentation of the patients can be due to the relative increase of the presentations by referral and can reflect also the result of the active search for cases promoted by the basic service. A reduction of the cases detected by examinations carried out in contacts has also occurred, pointing to a deficiency in the actions of the epidemiological tracking agency. That indicates the necessity of more attention to this aspect in

the actions developed for control of leprosy, since approaching these contacts interferes with the chain of transmission of the disease. According to Matos et al. the tracking of contacts, though it is a strenuous and difficult task, can bring tangible results to control and elimination of the leprosy even in highly endemic regions (MATOS et al., 1999). During period II a significant increase was observed in the rate of data not given, indicating a fault in filling out this information. However, when one compares the rates of data not given from period II with the results of a similar work carried out in Juiz de Fora between 1987 and 1995, whose rate was verified to be 13.4 %, it can be concluded that, in relation to the previous period, there was improvement in the system of data information (SOARES et al., 2000).

Regarding the clinical forms, the multibacillary form predominated in both periods (87 % in period I and 84.1 % in period II), being large when compared with the national rates (52,8 %). In fact, the results of the program for Leprosy Elimination Monitoring (LEM) (ORGANIZAÇÃO PAN AMERICANA DA SAÚDE, 2004) carried out in 2003, cite Minas Gerais, together with the States of Rio Grande do Sul and Goiás, as those which contribute most multibacillary cases in the country.

In spite of no statistically significant difference between period I and II, a percentage increase occurred in the clinical indeterminate form. When it is considered that the indeterminate form is thought to be the first clinical demonstration of leprosy (ARAÚJO, 2003), this result can mean a tendency for detection of more precocious cases and a better capacity of the services of basic attention in diagnosis and preventing incapacity. The proportion of tuberculoid cases, in relation to the sum of all the cases is also considered an indicator of tendency of endemic disease (FIGUEIREDO; SILVA, 2003). That is because 80 to 90 % of the healthy population presents a positive response to the Mitsuda test. This makes clear that during the expansion of an endemic disease, the tuberculoid form, which is the expression of a competent cellular immune response, becomes more frequent. Regarding the proportion of tuberculoid forms in the presented study, there was no difference between the periods (8.1 % in period I and 8.0 % in period II), indicating a tendency of stabilization of the endemic disease in the region.

As for the age curve, we observe its dislocation to the right, showing a tendency of diagnosis in patients with more advanced age. Nevertheless,

the disease continues to be more frequent between economically active individuals (45 to 59 years) in period II. The result found cannot be explained by the aging of the population since there was no significant difference in the age structure between the periods (IBGE, 2002). The detection of cases in older patients could be determined by the degree of efficiency of the control programs, since when the hidden prevalence is detected, it identifies patients whose cases are older and therefore, with more age. However, there was no intensification in control actions in the period evaluated, nor a significant increase in the rates of detection of new cases. Alternatively, an increasing age at onset may be due to an increasing of patients with long incubation periods, which is consistent with the predominance of multibacillary cases (IRGENS; SKJÆRVEN, 1985).

The rate of detection of new cases in patients under age 15, or the proportion of these to the total of new cases detected in the year, can signal the degree of endemic disease of the area. It indicates the precociousness of the exhibition and the persistence of the transmission of the disease when the values are above 0.5 per 10000 inhabitants, or above 5%, respectively. In this study the percentage of new cases under age 15 was 3.7%, and there was no difference between the 2 periods (ALBUQUERQUE; MORAES; XIMENES, 1989; CUNHA et al., 2007; IRGENS; SKJÆRVEN 1985).

When we compare the data in reference to gender, we observe in period I a predominance of the masculine sex and in period II, of the feminine sex. These data confirm a tendency for growth of the detection of leprosy at the cost of the feminine gender, already described in the literature (FIGUEIREDO; SILVA, 2003). That in part might be explained by a larger social mobility of women, thanks to their progressive insertion into the labor market in recent years, exposing them to greater risk. In addition, it may reflect the greater inclination of women to seek medical attention, or the lack of a mass screening program for leprosy.

In 2006, Moraes and others concluded that different genes are implicated in the resistance and sensitivity to the disease, such as tumor necrosis factor- α (TNF- α), interleukin-10 (IL-10), vitamin D receptor and parkin gene (MORAES et al., 2006). In the future, genetic tests might be used to track these markers in high risk populations, if they help

in the diagnosis of these patients and if they act to interrupt the chain of disease transmission and prevent neurological damage (BAKKER et al., 2006). The genetic mapping of *M. leprae* also contributes to inquiries regarding leprosy, bringing opportunities for resolving scientific questions about the disease and developing of new intervention tools (PENNA; PENNA, 2007).

In 2006, Bakker and others published the results of a study that suggests the use in highly endemic areas of the dosage of PGOL antibodies to identify serum positive individuals, the group with increased risk of developing the disease and more probability of transmitting the bacillus (BAKKER et al., 2006). The identification of these persons through serological tests might be a useful tool to interrupt the chain of transmission. Belgaumkar and others also suggests the use of recombinant IFN- γ and anti-IL-6 antibodies, aside from drugs and vaccines acting on cytokines wrapped in the immunopathogenicity of the disease, as a viable strategy in the combat of leprosy (BELGAUMKAR et al., 2007).

5 CONCLUSION

In this work we saw little changes in prevalence and incidence rates or in the clinical forms of leprosy identified in Juiz de Fora, MG. However, we did notice: a) an increase of the number of cases detected through the direction of health professionals; b) an increase in the age for opportunity of diagnosis; c) and a shift in gender from male to predominantly female cases. In spite of scientific and technological advancements it must not be forgotten that regional, cultural, socioeconomic and political factors need to be analyzed carefully in order to direct strategic decisions which could positively alter the epidemiological picture of the region. These actions are fundamental for control of disease transmission, without which it will not be possible to reach the goal of elimination of leprosy.

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