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Cojedes: a leprosy hyperendemic state

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Abstract

Background Leprosy is a chronic infectious disease produced by *Mycobacterium leprae*. In 1997 Venezuela reached the goal of elimination of leprosy as a public health problem (according to the World Health Organization a prevalence rate of ≤1/10,000 inhabitants), but five states still had prevalence rates over that goal. For this study we selected Cojedes State, where prevalence rates remain over the elimination goal.

Objective Evaluate the real leprosy situation in high-prevalence areas of Cojedes State.

Materials and methods Seven communities of Cojedes State were selected because they had the highest historic prevalence, as well as the highest prevalence in the year to be studied (1997).

Results A rank correlation using Spearman's test comparing historical prevalence rates (1946–1996) and detection rates (1998–2004) gave a statistically significant $P < 0.05$ value. Diagnosed leprosy cases were as follows: age: 3.2% under 15 years old; sex: male/female rates between 60% and 91.66% males. The highest number of cases were paucibacillary forms: indeterminate leprosy (33.07%) and borderline tuberculoid leprosy (32.28%); tuberculoid leprosy (7.00%); and multibacillary cases (lepromatous leprosy, LL) were only 2.36%. Bacteriologically, 18.52 patients were *M. leprae* positive. At the moment of diagnosis, 96.6% showed no disabilities, 3.4% showed grade I disabilities, and there were no grade II or III disabilities.

Conclusion This study confirms that several communities in Cojedes State have extremely high leprosy rates.

Introduction

Leprosy is a chronic infectious disease produced by *Mycobacterium leprae* with a historical background that extends to Before Christ epochs. It compromises the skin, peripheral nerves, and organs of the reticulo-endothelial system, and its clinical manifestations are determined by the specific immunological response of the host towards the *M. leprae* challenge.[1] Today, leprosy continues to be a public health problem that should be estimated not only by the number of cases but also by the important reactional phenomena and physical disabilities it produces, and by the stigma and social and psychological damages it involves, affecting patients' life quality, as well as in some cases, the well-being of the family group in endemic areas.

Man is considered as the only infection source; nevertheless, naturally infected animals (armadillos) have been found, and several laboratory animals have been experimentally inoculated (armadillos, mice, monkeys).[2] Patients with multibacillary leprosy (MB) have been considered as the main transmitters of the disease, but the role of paucibacillary patients (PB) in the transmission chain should also be considered.[3]

Leprosy occurs in the poorest countries and in the lowest socioeconomic levels; therefore, the influence of variables such as living conditions, nutritional status, concomitant infections, and previous infections due to other mycobacteria should also be considered as factors influencing the occurrence of the disease.[4,5] The study of genetic factors has shown that the disease is distributed in conglomerates, families, or communities, suggesting the possibility that these factors are also important. Multiplication of bacilli within macrophages can be determined by immunological mechanisms that involve antigen presentation (MHC complex) and HLA histocompatibility, both genetically determined. In the tuberculoid form, there is predominance of the HLA-DR2 and HLA-DR3 phenotypes, patterns related to susceptibility to the disease; in lepromatous leprosy there is predominance of

the HLA-DQ1 phenotype, also related to susceptibility. The presence of genetic variants in the promoter region shared by the PARK2 and PACRG genes has been recently identified as an important risk factor for developing the disease.[6,7]

Early detection and treatment with multidrug therapy (MDT) are considered to be the key elements for eliminating leprosy as a public health problem in endemic countries, alleviating the social and health losses produced by the disease. The benefit of significantly decreasing the number of cases also includes the decrease of the psychological sequelae in patients and their families, loss of work opportunities, and the cost for the community in compensating for financial losses (many of which are difficult to quantify).[8]

In Venezuela, the fight against leprosy began in the 19th Century with patient isolation measures, with scarce effect. In the 20th Century, in 1919, the first active search for cases campaign was organized and, as part of this effort, the Leprosy Hospitals of Cabo Blanco, in the Central Coastal Area, and at the Isla de Providencia in Zulia State, were created. At this time, control of the disease was still based on compulsory hospitalization of patients, isolating them from the community and their families with the purpose of decreasing transmission.[9] In 1936, with the creation of the Ministry of Health, a systematic leprosy control campaign was initiated. Important steps taken in 1945 were the use of sulfone therapy as specific treatment and the elimination of patient compulsory isolation. In 1946 the Ministry of Health created the Division of Leprosy, which later became part of the Department of Public Health Dermatology, with 31 Regional Public Health Dermatology Services distributed all over Venezuela.[10] The evolution of leprosy in Venezuela since 1946 is characterized by an increase of detection and prevalence in the years immediately following that date, due to the organization of the antileprosy program based on active finding and registration of cases. Later, from 1956 on, there is a gradual decrease of cases due to the effectiveness of sulfone therapy, control of household contacts, and early treatment of patients (Fig. 1).[11]

In 1982, due to drug resistance problems, the World Health Organization (WHO) instituted a program based on the use of supervised MDT, a combination of drugs that includes sulfone, rifampicin, and dapsone. This program has been applied in Venezuela since 1982, reaching a higher coverage in 1985, which at present is estimated

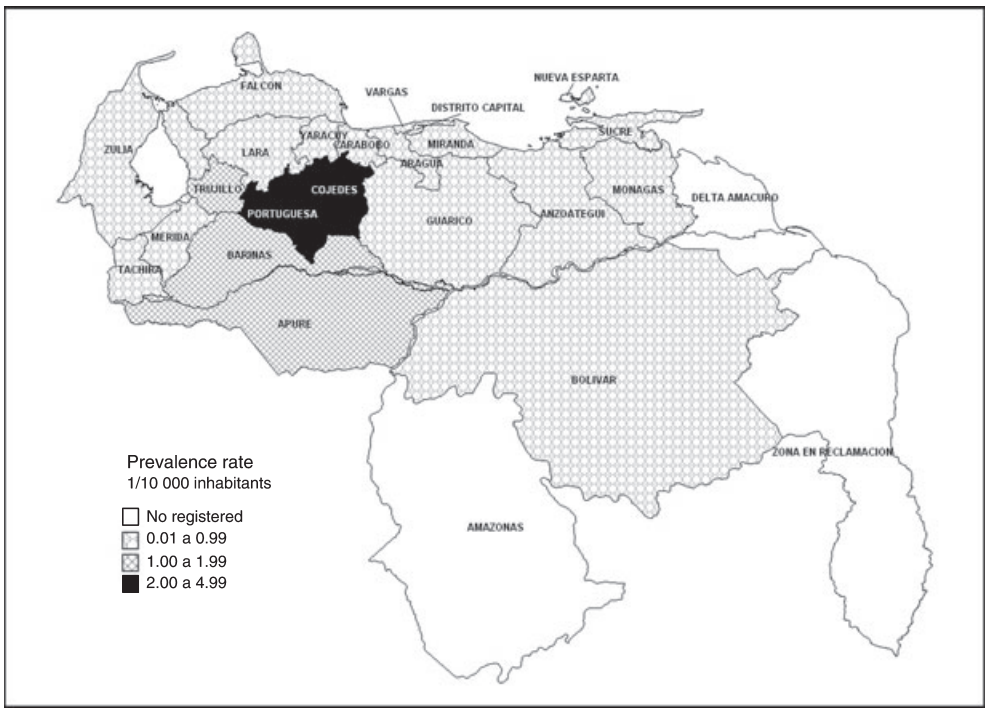

Figure 1 Prevalence of leprosy in Venezuela. Records from the Federal State 1999. Source: Computation Department. Instituto de Biomedicina, MPPS, UCV. Note: Venezuela reached the elimination rate established by WHO (prevalence rate 1/10 000 inhabitants or less) in 1997. Only four states (Apure, Barinas, Cojedes, Portuguesa) maintain prevalence rates over that limit. In 2002, Trujillo State also became part of the high-prevalence group

at 90%. To date, over 13,000 patients have been cured with this treatment scheme.[10,11] In the 1946–1996 period, there was a decrease of prevalence, with a more significant decrease in 1982 due to the installation of MDT and in 1995 due to registry updating.

In 1997, Venezuela reached the level of elimination of leprosy as a public health problem (according to WHO, a prevalence rate under 1/10,000 inhabitants). Only four states: Apure, Barinas, Cojedes, and Portugesa, maintained prevalence rates over the WHO elimination level. In 2002, Trujillo State, after an active search for cases, has also become part of this high prevalence group.[10,12] In 2008 the prevalence rate at a national level was 0.64/10,000 inhabitants, and in Cojedes State the rate was 3.40/10,000 inhabitants (Fig. 1). Special measures have been implemented in the states with the highest prevalence, including an intensive search for cases campaign. These measures have allowed identifying the hyperendemic populations included in this study.

Since the introduction of MDT for treatment of leprosy in 1982 by WHO, global prevalence has decreased from 5.5 million to less than 1 million (85%), but the detection rate has not decreased in the same way. In Venezuela, prevalence has decreased from 16.53 to 0.54 (91%), and the detection rate has remained with values oscillating between 0.21 and 0.30/10,000 inhabitants (Fig. 2). By the beginning of 2003, over 12 million cases had been cured worldwide; of 122 countries considered endemic in 1985, 110 were able to enter the elimination phase.[13] Worldwide, six countries concentrate the greatest leprosy prevalence: India, Brazil, Myanmar, Madagascar, Nepal, and Mozambique, representing 83% prevalence and 88% detection at a worldwide level, and the combined prevalence rate in these countries is 3.9/10,000 inhabitants.[14] In 2007, the Democratic Republic of Congo and Mozambique reached the elimination goal. There are a few countries such as Angola, Brazil, Central African Republic, Democratic Republic of Congo, India, Madagascar, Mozambique, Nepal, and the United Republic of Tanzania[15–17] that still have rates higher than the elimination rate.

The best way to analyze a leprosy therapy scheme is by determining the relationship of the disease with relapse rates, bacteriological index, morphological index, clinical response, etc. During 2000, 5266 relapses were reported in 79 countries; the countries that reported the largest number of relapses were India (4566), Nepal (125), and Indonesia (109). Recent data show that in 2008, 2985 relapses were reported in 49 countries; the countries that reported the largest number of relapses were Brazil (1433), India (325), Ethiopia (309), China (149), Nigeria (126), Indonesia (89), and Nepal (41).[14,17–20]

The latest data on new cases reported worldwide for 2009 were 249,007; 56% (140,390) were classified as MB, ranging from 52.29% in South East Asia to 82.54% in the Occidental Pacific area. Regarding age, 9.3% were children under 15 years old (23,161) with variations between 6.7% in the Eastern Mediterranean to 10.04% in Africa. Reported disabilities (grade II) varied in number: in the Eastern Mediterranean there were 17.45%; 11.6% in Africa; 10.1% in the Occidental Pacific; and 4.11% in Southeast Asia. The high disability percentage is attributed to late detection of new cases. In America, Brazil reported 6% grade II disabilities. Per gender, new cases reported in females were: 38.04% (1498) in the Eastern Mediterranean; 36.45% (10,868) in Africa; 24.82% (1454) in the Occidental Pacific area; and 35.45% (59,383) in Southeast Asia. In

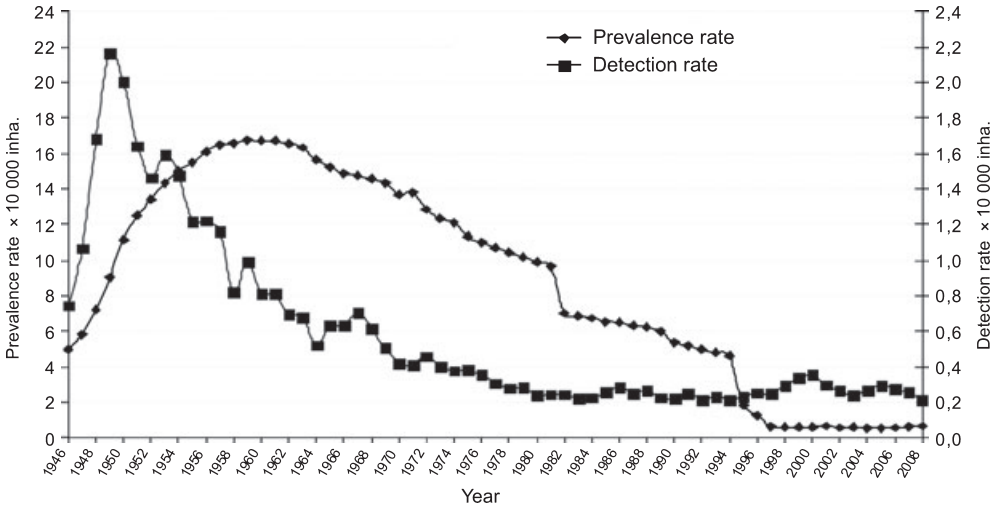

Figure 2 Prevalence and detection in Venezuela 1946–2008

America, new cases reported in females were: 40.93% (17,145).[20,21]

General objective

To evaluate the real leprosy situation in high-prevalence areas at a subnational level in seven communities of Cojedes State selected from 18 studied in the same period and in the same state.

Specific objectives

1 Determine the detection and prevalence rates in the selected communities.
2 Evaluate the clinical characteristics of the disease.
3 Determine the degree of physical disabilities present at the moment of diagnosis of leprosy patients.
4 Epidemiological characteristics of the endemia.

Materials and methods

Cojedes State was selected for being one of the states where the prevalence rate is higher than the national level.

The communities to be studied in Cojedes State were selected according to the historical case registry and prevalence during 1998–2004. The ones selected were those with the highest historical prevalence rates and with the highest prevalence rates during 1997. A sketch of each population was made, and each home was given a numerical order, indicating streets and important reference sites such as health centers, schools, church, etc.[21] Later, a socioepidemiological survey that included the whole family group was carried out, registering names, sex, age, relationship with the head of the family, family income, education, time of permanence in the area, and number of leprosy patients. Other concomitant diseases of the family group, such as tuberculosis, parasitic infections, etc., as well as the nutritional state, were also registered.[22]

In communities with <600 inhabitants, the convocation for the skin examination was done house-by-house at the moment of the epidemiological survey. In communities with between 600 and 9000 inhabitants, the convocation for the skin examination was done by loud speakers, local radio stations, and fliers, together with the participation of public health workers such as physicians and nurses. In three of the communities studied (Mapurite, Los Mangos and Santa Teresa), two and three active searches for case programs were done in subsequent years. In communities with more than 9000 inhabitants, the skin examination was done by epidemiological tracing of household and non-household contacts of diagnosed patients.

The physical examination consisted of skin examination looking for lesions suggestive of leprosy; neurological examination; thermal, tactile, and pain sensitivity tests; palpation of peripheral nerves; and histamine test in hypopigmented macules. In the anamnesis, the question "do you have any part of your body dormant or where you do not feel pain?" was asked. A bacteriological study and skin biopsy were performed on all persons with suspected leprosy to confirm the diagnosis. All data were registered in the patient's clinical case history according to a format used at the Instituto de Biomedicina. Bacteriological smears were stained with Ziehl-Neelsen and read by experienced technical workers according to the scale proposed by WHO.[10] The biopsy material was stained with hematoxylin-eosin and Fite-Faraco stains, and six consecutive sections were examined. The incapacity test was performed on all patients according to WHO schemes adapted by the Public Health Dermatology Services of the Instituto de Biomedicina.[10]

All diagnosed cases have been treated with MDT: six months for PB cases and one year for MB cases. In three of the communities studied (Mapurite, Los Mangos and Santa Teresa), an annual skin examination has been performed for three consecutive years.

Statistical analysis

Data with their respective frequencies were analyzed epidemiologically. The data were introduced in an Excel 2003 database, and a rank correlation using Spearman's test was performed. Detection data from historical registries (1946–1996) and those obtained during the study (1998–2004) were compared and considered significant ($P < 0.05$).

Results

Historically during 1946–1996, the community with the highest leprosy prevalence in Cojedes was Santa Teresa (15%), followed by Valoreño (11.8%), Los Mangos (11.2%), Las Tejitas (9.7%), Jabillal (7%), Mapurite (6.7%), and Garabato (4.7%), with rates over 400 per 10,000 inhabitants (Fig. 3). As far as detection, for the 1998–2004 period, these seven communities, of the 18 studied, remained with detection rates over 4% (Table 1).

Of the total number of inhabitants (13,210) in the 18 communities studied during 1998–2004, 9148 (69.3%) were examined. Of the seven selected communities, in five (Los Mangos, Mapurite, Santa Teresa, Las Tejitas and Jabillal) over 77.8% of the population was examined, and in the other two (Garabato and Valoreño), 57% of the population was examined (Table 2).

Of the total population examined (222/9148), 2.43% were diagnosed with leprosy, with rates between 20% in Los Mangos and 0.45% in Casa de Teja; showing rates over 3% in Mapurite (13.51%), Jabillal (5.41%), Santa Teresa (4.05%), Valoreño (3.6%), Las Tejitas (3.6%), and Garabato (7.6%; Table 3).

Spearman's correlation between historical rates (1946–1996) and the study rates (1998–2004) gave a statistically significant $P = 0.01$ value with a 0.959 rho (Table 4). Of the population diagnosed in the seven selected communi-

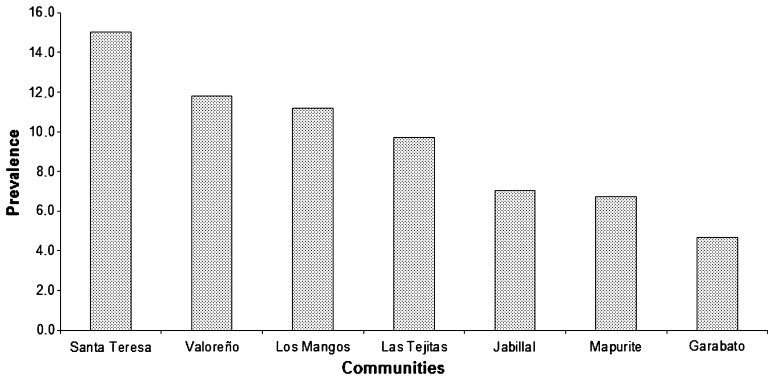

Figure 3 Historical prevalence records of leprosy in selected populations from Cojedes State, Venezuela 1946–1996

Table 1 Detection of leprosy cases in seven selected communities from Cojedes State, Venezuela, 1998–2004

Communities	Total population persons examined	Number of cases accumulated 1998–2004
Santa Teresa	45	9
Valoreño	60	8
Los Mangos	465	44
Mapurite	357	30
Garabato	257	17
Las Tejitas	111	7
Jabillal	211	12
Total	1506	127

Table 2 Populations surveyed and examined in 18 selected communities from Cojedes State, Venezuela, 1998–2004

Communities	General population	Population examined (PE)	% PE
Los Mangos	475	465	97.89
Retajao	273	259	94.87
Los Medanos	124	98	79.03
Las Tejitas	144	111	77.08
Santa Teresa	60	45	75.00
Mapurite	479	357	74.53
Caño Hondo	769	569	73.99
El Baúl	8500	5890	69.29
Urape	137	94	68.61
Garabato	385	257	66.75
Jabillal	327	211	64.53
Caujarito	142	84	59.15
El Genareño	296	165	55.74
Casa de Teja	273	147	53.85
El Muertico	539	271	50.28
Valoreño	127	60	47.24
El Perro	85	40	47.06
El Caño	75	25	33.33
Total	13,210	9148	66.01

ties, 73.2% of cases were under 15 years old, with rates varying between 60% and 91.66%. The rate of males who were under 15 years old is higher than that of females.

Of the 127 leprosy cases diagnosed in these seven communities, 21.26% had positive bacteriological smears as follows: Santa Teresa 1 (BB), Valoreño 1 (BL), Las Tejitas 1 (lepromatous leprosy, LL), Jabillal 2 (BL, LL), Garabato 4 (2 BB, BL, LL), Los Mangos 8 (5BB, 3BL), and Mapurite 10 (7BB, 3BL). Regarding clinical form, the highest proportion corresponded to PB forms (n = 100), especially indeterminate leprosy (IL) and borderline tuberculoid leprosy (BTL), with a low rate of lepromatous leprosy (LL), which only reached 2.36% and was reported only in El Baul, Garabato, Jabillal, and Santa Teresa (Table 5).

As for physical disabilities in the seven communities, at the moment of diagnosis 90.18% had grade 0 disabilities, 4.03% had grade I disabilities, and there were no grade II or III disabilities. The most frequent symptom observed was anesthesia in 87.03% of patients, with variations between 50% and 100% in the various communities, followed by plaques that were the most frequent clinical manifestation in 68% of patients, with variations in the various communities, but generally higher than 50% in most. The second most frequent clinical manifestation was hypopigmented macules in 30.8%, also with varying frequency per community. Nodules occurred in 5.4% of patients, and they were only reported in communities with more than 10 cases.

Discussion

Even though leprosy prevalence is less than one case per 10,000 inhabitants in most historically endemic countries after the implementation of MDT in 1982, 12 countries remain with levels higher than those established by WHO.[15,17] Nevertheless, the number of new cases remains stable, and there is preoccupation about occult

Table 3 Number of leprosy cases in 18 selected communities from Cojedes State, Venezuela, 1998–2004

Communities	Population examined	Percent of accumulated cases 1998–2004 (%)
El Caño	25	4.05
Santa Teresa	45	4.05
Valoreño	60	3.60
Los Mangos	465	19.82
Mapurite	357	13.51
Garabato	257	7.66
Las Tejitas	111	3.15
Jabillar	211	5.41
Urape	94	1.35
El Muertico	271	3.60
Caño Hondo	569	7.21
El Perro de Agua	40	0.45
Caujarito	84	0.90
Retajao	259	2.25
El Baúl	5890	20.27
Casa de Teja	147	0.45
Los Médanos	98	1.80
El Genareño	165	0.45
Total	9148	222 (2.43)

prevalence, defined as new cases expected that are not being diagnosed or are not diagnosed opportunely.[5]

Curtiss *et al.* analyzed prevalence rates as an indicator in leprosy control programs and concluded that the significance of this rate is of elimination but not of eradication.

Table 4 Historical 1946–1996 leprosy rates and 1998–2004 detection rates in 18 communities from Cojedes State

Communities	Historical case records 1946–1996	1998–2004 cases
El Caño	10	9
Santa Teresa	9	9
Valoreño	15	8
Los Mangos	53	44
Mapurite	32	30
Garabato	18	17
Las Tejitas	14	7
Jabillal	23	12
Urape	4	3
El Muertito	10	8
Caño Hondo	31	16
Perro de Agua	2	1
Caujarito	5	2
Retajao	7	5
El Baúl	67	45
Casa de Teja	2	1
Los Medanos	6	4
Genareño	2	1
Total	338	222

Correlation coefficient rho = 0.959, $P < 0.01$, statistically significant.

Table 5 Distribution of leprosy cases according to clinical forms in seven selected communities Cojedes State, Venezuela, 1998–2004

	Clinical forms					
Communities	IL	TL	TB	BB	LB	LL
Santa Teresa	4	1	3	1	0	0
Valoreño	2	1	4	0	1	0
Los Mangos	18	6	12	5	3	0
Las Tejitas	1	5	0	0	0	1
Jabillal	2	2	6	0	1	1
Mapurite	7	1	12	7	3	0
Garabato	8	1	4	2	1	1

Total number of cases = 127.
BB, borderline borderline; IL, indeterminate leprosy; LB, leprosy borderline; LL, lepromatous leprosy; TB, tuberculoid borderline; TL, tuberculoid leprosy.

Eradication only by MDT is extremely difficult, considering that a large number of persons present subclinical infections,[23] i.e. they have been infected by *M. leprae* but they have not developed symptoms of the disease. This means that research and vaccination programs have to be established to lead not only to elimination but to the eradication of the disease.[24]

In most of the endemic countries that have reached the elimination phase, there are still certain communities with high prevalence rates, as is the case of Venezuela, where five states (Apure, Barinas, Cojedes, Portuguesa, and Trujillo) report rates higher than one case per 10,000 inhabitants. In Cojedes State, there are communities that historically have shown high leprosy prevalence and, when an active search was done, this finding was confirmed. When correlating cases detected according to historical registries (1946–1996) with cases registered during the study period (1996–2004), a highly significant correlation was determined, suggesting that leprosy distribution in the different communities of the study area has not changed from the historical rates.

The coverage of the population examined was high when the approach was a house-by-house search in small communities; on the other hand, in a larger community (El Baúl) there was 14% coverage because the approach was through communication media, which indicates that the best results are obtained through an active house-by-house search, even though its cost is higher. It is a priority in communities with larger numbers of inhabitants to design health education programs in an effort to obtain greater community participation for the attendance to skin examination. The various communities have different populations, therefore a single cost–benefit method should be designed to cover these different areas.

These communities behave differently from larger communities; therefore, hyperendemic areas were kept under permanent surveillance, and cases were detected through active house-to-house search for cases activities. Our leprosy program is directed towards early detection and treatment, and control and examination of contacts has produced an important decrease of grade II and III disabilities.

Case detection in the 18 communities studied was very high (4.5%), and in a short period of time (1998–2004), it was possible to diagnose a number of cases equivalent to two-thirds of all the cases that had been diagnosed in 40 years of historical registry (1946–1996; 222 vs. 338, respectively). Bhatki and Singh published a similar study carried out in India where 5000 non-medical or paramedical persons were prepared to evaluate large hyperendemic communities in Bombay, where 1.83 cases per 10,000 inhabitants were identified from a population of over 11 million persons studied.[25]

In most communities with smaller numbers of inhabitants, detection rates were very high, implying a community transmission route, where the respiratory route would play a very important role, in contrast with the household transmission route, where the respiratory route and the permanent person-to-person contact would be involved.[26] Differences in the circulating bacteria in the area could also be involved.[27]

These detection rates are much higher than those seen in other parts of the world. This can be explained in two ways: use of search methods where specialists in dermatology intervene; and community transmission. In the Santa Teresa community, with 20% detection, there are only 60 inhabitants in 11 homes, followed by Valoreño with 13.2% detection where there are 120 inhabitants in 25 homes. These very high rates can be a problem of permanence of rates due to the small number of persons living in these communities in intimate and permanent contact.

The distribution in two large age groups reveals a high proportion in children under 15 years old, which agrees with what has been reported in India and Brazil.[14,28] This finding can be attributed to the early diagnosis obtained through the approach form used. Due to this, the leprosy program will insist on active search for cases activities in highly endemic areas as the most effective measure to stop disease transmission. The male predominance seen in the under 15 years old group corresponds to what has been described by Lombardi and Suarez,[29] where this gender present a higher risk due to their greater mobility and contact opportunities. Nevertheless, other factors such as the permanent close contact with scarce mobility of these persons should be investigated in small hyperendemic communities.

Regarding bacteriology, the low positive percentage observed (21.3%) in the seven selected communities is related to the clinical type of the disease found, with predominantly PB forms that represent 75% of cases in these communities, implying an early detection and emphasizing the importance of an active search for cases program, for early diagnosis and prevention of social stigma and disabilities.

The physical disabilities observed in a small number of the cases diagnosed in the seven communities were mild: most of them were grade 0 (96.6%) or grade I (3.4%), and there were no grade II or III disabilities, which are usually seen when diagnosis is delayed. According to WHO data, disabilities have particular characteristics in different countries: in Mozambique the main characteristic is the high proportion of grade II disabilities in newly diagnosed MB cases; while in India there is a high proportion of grade I disabilities; in Brazil up to 75.4% disabilities are reported, 7% of which correspond to grade II and III, where deformities have already occurred.[14,30]

The most frequent clinical forms found were the PB forms [IL, tuberculoid leprosy (TL), BTL], similar to what is seen in India and some African countries. For 2001, of the 675,180 new cases reported worldwide, 39% (261,713) were classified as MB and 52% (352,347) as PB. The proportion of MB cases is high in the East Mediterranean and Occidental Pacific areas and especially low in South East Asia.[14]

The PB clinical forms predominantly found in our study appeared with anesthetic and hypopigmented areas, and they could be interpreted as initial forms of the disease due to early detection, lesions corresponding to TL and BTL reflect the immunological status of the patient and the direction taken by the disease.

Early diagnosis is one of the major problems for the control of leprosy and, due to this, it is increasingly important to find specific molecular markers for the bacillus, which would facilitate an early diagnosis and opportune treatment, influencing the interruption of transmission.[31,32]

After all cases diagnosed received MDT immediately after diagnosis, the communities were newly evaluated in subsequent years, and new cases appeared in persons already examined, which reflects the variable incubation periods of the disease and the maintenance of the transmission due to factors that need to be studied. On the other hand, due to the protection given by the BCG vaccine, and the experience with combined vaccines,[33] a true eradication campaign should include vaccine programs in these hyperendemic areas, as well as the study of other risk factors such as overcrowding, poverty, and poor sanitary conditions. Due to this, the Instituto de Biomedicina has begun a social development project in communities

affected by endemic diseases within the frame of the Center of Excellence in Apure, Cojedes, and Portugesa.

Conclusions

Even though Venezuela has been at the elimination of leprosy as a public health problem level as established by WHO since 1997, there are still some hyperendemic communities that should be subjected to extensive study to determine the reasons for the continuation of the endemia. The studies carried out in Cojedes State confirm the high leprosy prevalence in these areas, and the early detection in this state seems to indicate that the clinical forms of anesthesia and hypopigmented macules are the early-onset forms of occurrence of the disease, before it leans to either pole, depending on the immunological status of the patient. Two transmission forms are identified: the orthodox household form, and the community form, where all the inhabitants are in contact. In small communities, the house-by-house approach carried out by the local health authorities could be the most effective detection method. Our work shows that with an early clinical diagnosis and opportune treatment, the number of patients with disabilities is importantly reduced.

Through the study of the mycobacterial genome, in the future perhaps we could introduce the use of immunotherapy using specific protective epitopes for the complete eradication of the disease.

This study presents some epidemiological and clinical aspects observed in certain communities of Cojedes State, considered as a hyperendemic state. Nevertheless, we recognize that this disease may be strongly related to other important aspects, such as social and environmental situation, possibly different bacterial species circulating in the area not recognized until now.

This paper constitutes a precedent for the continuation of studies in the various communities approached, of great relevance for their post-treatment surveillance.

Acknowledgments

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