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Original

Impact of Hansen's disease on relatives of patients in Costa Rica

Ana Rivera-Chavarría, [1]Germana Sánchez-Hernández, [2]Azálea Espinoza-Aguirre [3]

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Abstract

Aim: Family transmission of Hansen's disease is a well-established fact; although transmissibility is low, intra-household contacts of untreated sick people are a high-risk group. The objective of the study was to identify common sociodemographic, cultural, and clinical characteristics in family groups with a history of Hansen's disease, as an input to improve leprosy treatment.

Methods: A qualitative study was conducted, using the technique of semi-structured in-depth interviews, based on an interview guide developed, and taking as reference sociodemographic, social, and cultural factors related to diagnosis and treatment. Twenty-five adults between 23 and 88 years of age, of both sexes, serviced by the Costa Rican public health system were selected. Genograms were used to identify family members with a history of the disease.

Results: The study showed that 12 participants came from 3 family groups; two groups with three generations affected. The participants were diagnosed at economically active ages of life. In addition, they were engaged in manual occupations, with low educational levels and the Christian religion. At the time of the interview, they were aware of the family history. The clinical presentation in the three family groups was lepromatous leprosy. One case of spousal leprosy was identified, and one 15-year-old female participant was diagnosed.

Conclusions: The study identified common sociodemographic, cultural, and clinical characteristics of family groups, which showed the need to strengthen contact surveillance in families with new cases.

Keywords: Leprosy, prevention, family relationships, Costa Rica.

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Familial transmission of leprosy or Hansen's disease (HD) is well established.[1] The transmission dynamics of *Mycobacterium leprae* and *Mycobacterium lepromatosis* (the causative agents of leprosy) are complex. The upper respiratory tract is considered the main portal for entry and exit of *M. leprae* and people with active disease are the main sources of infection [2] For *M. lepromatosis* the mechanisms are unknown and interactions with unknown reservoirs may occur in non-endemic areas. [3]

Compared to the general population, household contacts of HD patients are a high-risk group for contracting the disease and suffering the effects of HD. [4]Numerous studies have shown that most new HD patients have a history of contact with another patient. [5,6]

Authors' affiliation:
[1] Costa Rican Institute of Research and Teaching in Nutrition and Health, Health and Nutrition Unit (Inciensa).
[2] Independent Researcher, Social Anthropology, Costa Rica.
[3] Health Surveillance Direction, Ministry of Health of Costa Rica.

Abbreviations:
CCSS, Caja Costarricense de Seguro Social; HD, Hansen's disease; MB, multibacillary leprosy.

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✉ arivera@inciensa.sa.cr

Due to its broad spectrum of clinical manifestations, the classification of HD is complex and may include clinical, histopathological, microbiological, and immunological features proposed by the Ridley and Jopling classification. [7,8] To facilitate its management, the Pan American Health Organization (PAHO) / World Health Organization (WHO) classified HD according to the number of lesions, several nerves affected, and bacillary load into multibacillary (MB) and paucibacillary.[7] The risk of developing the disease among paucibacillary contacts is 2-3 times higher than in the general population, while the risk increases to 5-10 times among MB contacts. [9]

There is therefore a greater chance of becoming infected with Hansen's bacillus and developing the disease when there is repeated, intimate contact, most evident in childhood HD cases, especially mother-child contact, and transmission between partners.[10,11] Innate predisposition to infection seems to be particularly crucial for HD: it is estimated that only a small fraction (5-12%) of people exposed to *M. leprae* become successfully infected. [12]

During the period 2012-2017, 51 new cases of HD were registered in Costa Rica with a national prevalence of 0.06 cases per ten thousand inhabitants.[13] The annual detection in the last decade was 9 individuals per year.[13] The provinces with the highest prevalence of HD are Puntarenas, Limón, and San José (20, 10, and 9 cases, respectively). According to the HD drug recall registry, 90% correspond to MB HD.[13] No cases of childhood leprosy have been reported in the country since the 1990s.[14] Despite the low prevalence of HD at the national level, there are delays in diagnosis[15], which have physical, psychological, and economic consequences for the patient and his or her family.

The objective is to identify common socio-demographic, cultural, and clinical characteristics in family groups with a history of HD, as an input to improve HD treatment as part of the main study "Factors associated with leprosy treatment delivery in Costa Rica".

Methods

A qualitative study was conducted, using the semi-structured in-depth interview technique, which explored factors related to seeking treatment for HD. Twenty-five adults between 23 and 88 years of age, of both sexes, who were assisted by the Costa Rican public health system, were selected. The selection of informants was made through a deliberate selection and by opportunity, according to the following inclusion criteria: older than 18 years, of both sexes, having suffered from leprosy or suffering from leprosy and who were willing to participate in the study by signing the informed consent form.

The data was collected using the in-depth interview technique, which was used by the team's social anthropologist from July 2016 to July 2018, to investigate, based on an interview guide prepared in advance and taking as a reference sociodemographic, social, and cultural factors related to HD diagnosis and treatment.

To complement the data obtained in the in-depth interview, the clinical records of each participant were reviewed, for which a data collection sheet was prepared that included sociodemographic, demographic, and clinical factors of the first consultation and subsequent consultations. To identify the degree of disability, the records were consulted according to the medical note where the degree of disability could be inferred according to the WHO disability classification system into 3 degrees: 0, 1, 2 (Disability in people affected by leprosy: the role of impairment, activity, social participation, stigma and discrimination, Van Brakel WH *et al.*, Global Health to Action, 2012).

The textual transcripts of the interviews constituted the unit of analysis. They were classified and coded according to the objectives of the study and the dimensions addressed. The analyses were carried out using the Ethnographic program (Version 6 Qualis Research) combined with the manual information coding technique. The analysis consisted of 1) coding of broad nodes (dimensions), 2) distinction of specific information to identify common, divergent, and emerging elements, 3) comparison and condensation of information.

To ensure the internal validity of the study, the transcripts were reviewed four times (once by each researcher and once by the work team). In addition, textual sentences were selected to illustrate the central content of each category while maintaining confidentiality.

The data from the files were coded, analyzed, and compared with the data from the individual and group transcripts using Excel.

The genogram is an instrument that allows a broader understanding of the family environment in which the participants arise and develop. It requires the use of symbols and figures to represent members, structure, and important events such as diagnosis and age when diagnosed with HD. [16]

The following information on the participants and their respective family groups was used for data collection: family identity data (sex, age, family members, such as parents-children, siblings, grandparents, marriages, and deaths); data on the index case (corresponds to the first case reported to the health authority that gives rise to the attention of the researcher and originates a series of actions necessary to determine the focus of infection[17]); data on cases in the family (corresponds to the cases of HD after the index case); HD in the family nucleus (corresponds to the HD cases documented in the family).

The study had the approval of the National Council of Health Research (CONIS) because it was considered an institutional task of the Ministry of Health, based on the provisions of Article 7, paragraph a) of the Biomedical Research Law (Law 9234). In addition, with prior authorization from the Bioethics Committee of the Center for Strategic Development and Information on Health and Social Security of the Caja Costarricense de Seguro Social (CENDEISSS, CCSS), access was obtained to the clinical file of the participants, so that the results obtained from the interview would be complemented with the data recorded in the file regarding the use of services and compliance with treatment.

Due to the participation of Inciensa's researchers, we had the approval of Inciensa's Scientific Ethical Committee. The interviewees consented to participate by signing the informed consent form. To guarantee the confidentiality of the stories, the participants were identified as E1, E2, E3.... E25.

Results

Twenty-five interviews were conducted with a total of 25 participants. One participant had to be excluded from the study because he was discarded as an informant by the dermatology specialist.

The average interview time for this study was 67 minutes. The 24 participants ranged in age from 23 to 88 years old and 7 of them were female. Regarding marital status: 7 were single, 13 were married, and 4 were cohabiting, and 18 participants practiced Christianity.

Twenty-eight records from second and third-level hospital centers of the CCSS were reviewed because four informants had duplicate clinical records.

Of the 24 participants, 18 individuals had a documented positive family history of HD. In turn, 12 participants came from three family groups: two family groups with three affected generations. In one family group, one case was identified where the couple was infected. The three family groups are described below:

Description of family #1

Family #1 is described as a nucleus in which at least 3 generations with members of both sexes with HD can be identified, five of the participants in the study (see Figure 1). The clinical characteristics of family #1 are described in Table 1.

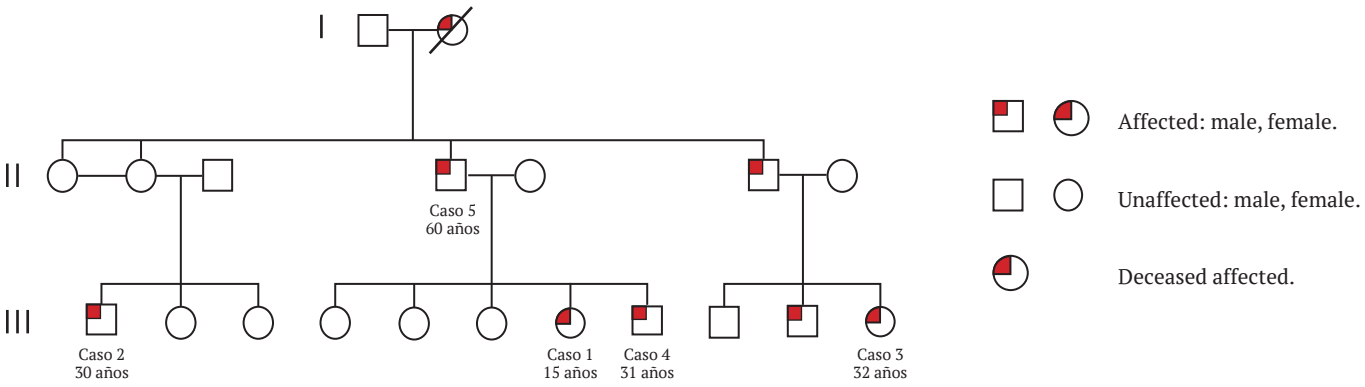

Figure 1. Genogram of family #1.

Table 1. HD Clinical Characteristics of Family # 1

Case No.	Sex	Age (diagnosis)	Evolution (years)	Type of HD	Degree of disability**
1	Female	15	2	LLD, MB	G1
2	Male	32	3	LLN, MB	G1
3	Female	33	2	LL, MB	G2
4	Male	31	2	LLD, MB	G2
5	Male	60	33	LLD, MB	G1

LLD: Diffuse Lepromatous Leprosy, LLN: Nodular Lepromatous Leprosy, LL: Lepromatous Leprosy, MB: Multibacillary. **: G= Grade.

The index case (case 1) of family # 1 corresponds to a 15-year-old female from Cartago, Catholic, single, incomplete secondary school, household occupation, who consulted the local clinic in 1995 because of skin lesions on the lower limbs. During the interview, it was established that her grandmother, father, uncles, aunts, brother, and some cousins were carriers of HD. This information was corroborated by the in-depth interviews with the participants and the review of their files. This is how the participant describes it: *"grandma had the disease, daddy's disease, and grandma's disease, I think her grandmother had it because there (...) that has something to do with daddy's genetics or something". (E 23, female, 37 years old).*

In February 2012, a 32-year-old male participant (case 2) resident of Limón, Catholic, gardener, primary school graduate, married, was diagnosed, and referred to a third-level hospital due to a three-year history of skin lesions; he was the first cousin of the index case. By recommendation of case 1, the participant informed the treating physician of the family history. This is what he says after having consulted on multiple occasions at the first level of care receiving different treatments and without an adequate diagnosis: *"See doctor, in the family we have a problem, I tell you in the family, my sister, my cousin, I have 2 cousins I tell you, 3 cousins, and 2 uncles of mine who have suffered from a disease called Hansen's disease" (E14, male 37 years old).*

Female 33 years old (case 3), the first cousin of case 1, 2, Christian, agricultural worker, single, finished primary school, Limón resident, diagnosed in 2015. She reports one year of the evolution of skin lesions on the lower limbs, thorax, anterior abdomen, and arms. The participant did not know the history in her family, it was only in a subsequent consultation with the dermatology specialist that she discovered that her father, brother, paternal uncle, and paternal grandmother suffered from HD. This is what she says in her story: *"I asked my dad and my dad told me that when I was 4 years old, he was discharged from that disease (...) Yes, the grandmother, his mother (the father). My brother. Also, my dad's brother. (E20, female, 37 years old).*

In 2016, the 31-year-old male participant (case 4) was diagnosed. He was in cohabitation, had completed primary school, was a factory worker, and brother of case 1, first cousin of cases 2 and 3, and was referred to a third-level hospital with skin lesions on his lower limbs with macules, scars, and ulcers, and was a resident of Cartago. In his story, he mentions the family history: *"There are about ten or nine. Ten, ten: the grandmother (my grandmother started), his father, an uncle, his sister, him, a cousin (...) a cousin". (E4, male, 31 years old).*

Male, 60 years old when diagnosed (case 5), Catholic, married, farm laborer, resident of Cartago, father of the index case and case 4; paternal uncle of case 2 and 3 with 60 years of age when diagnosed, he was again detected in the contact study of case 4 in 2016 (diagnosed with HD in 1983 but abandoned treatment). This is how he relates it in his story: *"The deceased my mother was going to the hospital, and he (brother) was also going. After a few days, I started to travel with them, they were discharged and I continued, it was when there was that little problem that I did not come back". (E13, male, 60 years old).*

Description of Family #2:

Family #2 is described as a nucleus in which three generations with members of both sexes with HD are identified, 4 of the participants in the study (Figure 2). Interviews with participants and file review revealed that the father-in-law of case 1 and paternal grandfather of cases 2, 3, and 4 had

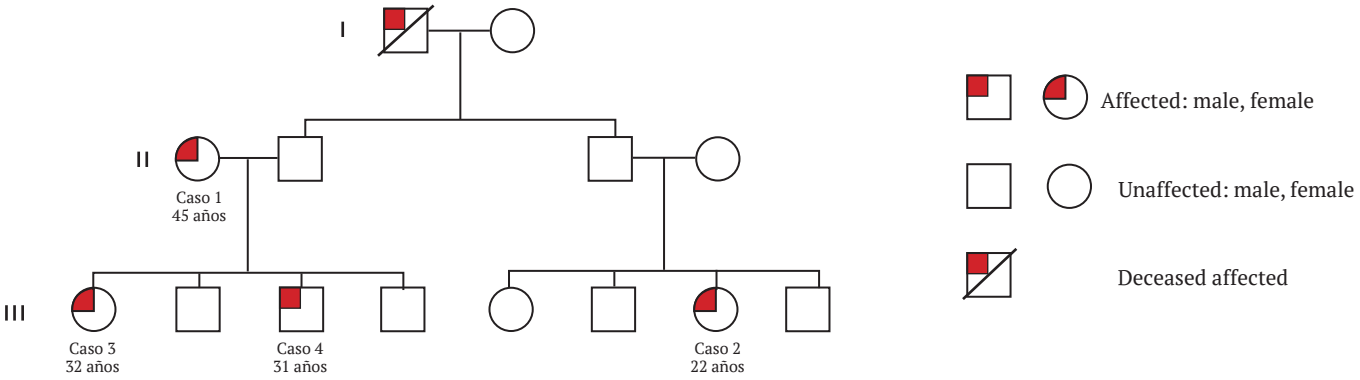

Figure 2. Genogram of family #2 with Hansen's disease.

Table 2. HD clinical characteristics of family #2

Case No.	Sex	Age (diagnosis)	Evolution (years)	Type of HD	Degree of disability**
1	Female	45	2	LLD, MB	G2
2	Female	22	3	LLD, MB	G1
3	Female	32	2	LLD, MB	G1
4	Male	31	1	LLD, MB	G1

LLD: Diffuse Lepromatous Leprosy, LLN: Nodular Lepromatous Leprosy, LL: Lepromatous Leprosy, MB: Multibacillary.
**: G= Grade.

HD. The clinical characteristics of family #2 are described in Table 2.

The index case (case 1) of family # 2 corresponds to a 45-year-old female, resident of the province of Alajuela, married, housewife, Catholic, who consulted a level 3 national hospital in 1996 for ulcers in her lower limbs. In her speech, she refers to other family members with the disease: *"When this niece of mine told me that she had it, I remember that I was at home when they called me. Her mother said to me, 'Do you know what my daughter has? And I said to her, 'What, what did she come out with? She told me, she has leprosy (...) because according to what the doctors tell us is that (the cause of leprosy) is the kids' lack of defenses, so I think, then my two children were without defenses, only a few defenses, and the others do have more". (E24, female, 56 years old)*

Female participant, 22 years old when she was diagnosed with HD (case 2). In 2012 (22 years after the index case), married, resident in the province of Alajuela, Catholic, housewife, consulted a private doctor for infertility, spots on her feet, and anemia. This is how she relates the family history: *"Yes, at that time we told him (the doctor) when he told us, he couldn't find a way to tell us that it could be that disease, and then we told him that it could be, because I had an aunt, and my mother had taken care of her when she was like that, and she had sores and everything, my mother was the one who cured her and I was very young, so it could have been there I caught it". (E3, female, 26 years old).*

Case 3 corresponds to a female participant 32 years old when diagnosed (in December 2015), resident of the province of Alajuela, daughter of Case 1, single, complete primary school, operator in a packing plant, Catholic, who was seen in a third-level hospital for symptoms of cutaneous vasculitis, in lower limbs, madarosis, anesthesia and anhidrosis that had been present for 2 years. In her story she describes the history and the contacts in the family as follows: *"From my house, there are two of us, they are all already checked and they are all (...) I am not going to lie to you that there is only one that we have not been able to do because we have not had the opportunity to take him, but the doctor already told me there, that if he had it, something would have already happened to him." (E25, female, 34 years old).*

Case 4 corresponds to a 31-year-old male when diagnosed, resident of the province of Alajuela, complete primary education, businessman, married, Catholic, who in September 2015 began with ulcerations in the lower limbs suggestive of

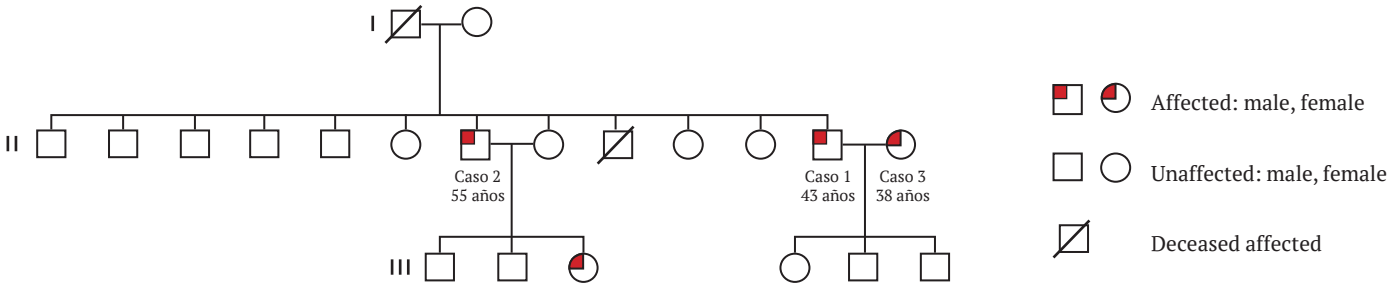

Figure 3. Genogram of family # 3 with Hansen's Disease.

Table 3. HD Clinical Characteristics of Family # 3

Case	Sex	Age when diagnosed	Evolution (years)	Leprosy Type	Disability** Disability
1	Male	43	5	LLD, MB	G2
2	Male	55	3	LLN, MB	G2
3	Female	38	SD	LL, MB	SD

DLD: Diffuse lepromatous leprosy, DLL: Diffuse lepromatous leprosy, DLL: Diffuse leprosy, LLN: Leprosy LLD: Diffuse Lepromatous Leprosy, LLN: Nodular Lepromatous Leprosy, LL: Lepromatous Leprosy, MB: Multibacillary. **: G= Grade. SD:no data.

vasculitis process was referred to a tertiary hospital and edema of six months of evolution with positive epidemiological links (mother, sister, and cousin). *"Because my mother had it, a cousin who was always in contact with us had it, my sister had it, and now I have it. (E2, male, 32 years old).*

Description of Family #3

Family #3 is described as a core family with two generations of male and female members with HD, three of whom were participants in the study (Figure 3). The clinical characteristics of the members of family #3 are described in Table 3.

The index case of family # 3 corresponds to a 43-year-old male, diagnosed in 2008, resident of Puntarenas, married, completed primary school, Christian, taxi driver, with 5 years of evolution of dysesthesias, anesthesia in extremities, episodes of ulcers in lower limbs, and hair loss in extremities, trunk, eyebrows, and eyelashes. Concerning family history, the participant refers to the following: *"Only one has appeared and that is my wife. My brother came after me. However, he is quite affected, because, as I said, he had other symptoms, it affected his bones. However, he works, he goes around working." (E8, male, 43 years old).*

Case 2 of Family 3 corresponds to a 55-year-old male when diagnosed in 2012, a resident of Puntarenas, a farmer, married, Catholic, incomplete secondary school, with a 3-year history of paresthesias and dysesthesias. The participant is the brother of the index case of family # 3. He mentions the sick family members with HD as follows: *"It turns out that the first one to come out with this was the younger brother, yes, the youngest. About 5 or 6 years before (...) yes, and his wife has already received treatment for the same disease. (E21, male, 55 years old).*

Female participant, 38 years of age when diagnosed (case 3), resident of Puntarenas, married, Christian, waitress, completed high school, with macular, hypoesthetic lesions that had evolved for months, in the year 2014. The participant is the wife of case 1 of family # 3. In her story, she describes the members of her in-laws' affected with the disease: *"The brother and a niece. A daughter of my brother. They had it, but they have finished treatment.* (E22, female, 38 years old).

Discussion

The analysis identified common sociodemographic, cultural, and clinical characteristics in the

three family groups of participants with a history of HD, which are like those findings in high-prevalence countries.[1,2] The common characteristics identified constitute an input to improve timely treatment and diagnosis at the national level.

From the analysis of the sociodemographic data, following the literature published in Brazil,[18,19] it is observed that the participants with a positive family history of HD were diagnosed during the most economically active periods of their lives. One participant who was diagnosed at 15 years of age also stands out, which reflects active transmission and a state of hyperendemicity within the family group.[20] It should be noted that, since 1998, there have been no reports of cases of people under 15 years of age at the national level. [13,14]

Studies on HD and its possible association with gender have reported a high prevalence in males.[21] A recent study published by Alvarenga *et al*. showed that the heterozygous genotype of the TLR1 gene is a female-specific protective factor. However, the mechanisms and signaling pathways that guide this effect, as well as the role of sex hormones in HD protection, are still unclear and require further research to be elucidated. [22]

Most of the family members are in manual occupations, have a low level of education, and are family contacts of an HD patient, which, according to a recently published meta-analysis on HD are risk factors for developing HD.[21]

Religion has proven to play an important role in other stigmatizing diseases, such as human immunodeficiency virus infection.[23] In the specific case of HD, old fears and misconceptions about the disease have proliferated for centuries and the condition remains a problem of social stigmatization, so health education campaigns should inform about HD through messages that sensitively address beliefs and misconceptions in the local community.[24]

From the analysis of the qualitative data, between 4 and 8 cases can be identified in each family group. All the participants at the time of the interview were aware of the family history. However, at the time of diagnosis, most did not suspect that they might be suffering from this disease (except for two participants). This may have contributed to late diagnosis and complications.

Physical disabilities represent the main challenge of HD; the number of cases with grade 2 disability at the time of diagnosis suggests that the efforts made to achieve early detection of HD are still not sufficient. This situation is described in countries with high endemicity as in those that have achieved the figures of elimination of the disease, so there is a risk of reversing the progress made in the specific case of Costa Rica.[22-24]

It is important to note that some participants told the treating physician about their family history of HD. In some cases, participants were persuaded by other family members to tell the treating physician that they had a family history of HD. Others, even though they knew of the history, concealed it from the doctor for fear of having the diagnosis confirmed. This contributed to a delayed diagnosis. On the other hand, the fact that HD was declared eliminated from Costa Rica in 1995[12] as well as the disease´s low prevalence, most likely contributes to the cognitive bias of the medical staff;[25] a reason why it has not been included as a probable diagnosis and why it has not been questioned in the family history, nor is long-term follow-up given to family members. In addition, the declaration of elimination of HD has resulted in a diversion of attention to other public health problems. Consequently, human and material resources devoted to HD control have declined, along with public interest in the disease and the internal and external financial support for HD control.[26]

The literature suggests that Lepromatous Leprosy (the clinical classification form in the three family groups shown in the article) has long incubation periods or long exposure periods that favor the risk of transmission between contacts [27] (Tables 1, 2, 3). Two of the index cases mentioned in the three family groups were diagnosed with lepromatous leprosy more than 30 years ago and another index case 16 years ago. Since these periods, there have been recent cases in all three family groups, indicating that the risk of developing the disease depends not only on the bacillary form of the index case but also on the proximity to the index case, since the risk increases in household contacts and consanguinity with the index patient, due to a genetic susceptibility to develop HD.[28] Because of the long and imprecise incubation periods of HD, it cannot be determined which contact will ultimately develop the disease.[4] Therefore, strict adherence to the Standards of Care and Control of Hansen's

disease, as well as strengthening contact surveillance efforts in families with new cases of HD, as suggested in countries such as Brazil, is essential.[29] The family history should be recorded and registered for proper follow-up in the Single Digital Health Record (EDUS), so that the information is not left behind and is available when needed.

Despite continuous and prolonged contact, spousal leprosy is not frequent and requires several years to develop in the second person,[30] the study identifies a case of spousal transmission. Coincidentally with the literature, the study shows lepromatous leprosy as a clinical form of presentation in the index case of family # 3, constituting a possible predisposing factor for the spouse to develop HD[8] among other possible variables.

The limitation of this study is that some participants talked about an event that happened in the past, which could have led to a recall bias. Qualitative and quantitative studies are needed on HD knowledge biases in HD family groups and health personnel, risk factors, as well as the role of some social actors, and the opportunity for cooperation with health services.

In conclusion, the results of this study show that the follow-up of contacts in health services is a permanent challenge due to the long incubation period and the stigma associated with the disease. Within this context, a national standard of care is in place that establishes identification and follow-up for a certain period for both the person with HD and their contacts. However, as identified in the analysis, this standard was not always met, which contributed to participants not knowing the family history to facilitate timely diagnosis. Intentional case finding among contacts should be incorporated as an effective method for early diagnosis of HD in households, which could reduce the sources of infection and break the chain of transmission.

All family members should be informed about HD to prevent any of them from keeping it hidden. This would also help to manage the stigma of the disease.

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