Close Contacts with Leprosy in Newly Diagnosed Leprosy Patients in a High and Low Endemic Area: Comparison between Bangladesh and Thailand

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ABSTRACT

Background: As part of a larger study of the role of close contacts in the transmission of *M. leprae*, we explored whether the proportion of newly detected cases with a family history of leprosy differs with different incidence rates of leprosy in a population.

Methods: Retrospective analysis was performed of contacts of all new leprosy patients diagnosed during a 10-yr period in well-established leprosy control programs in Thailand and Bangladesh. By our definition, a contact group consisted of the new case and of past and present cases who were relatives and in-laws of the new case. For a new case, the nearest index case was defined on the basis of time of onset of symptoms for the cases in the contact group, in combination with the level of closeness of contact between these cases and the new case. Three contact levels were distinguished. In Bangladesh these levels were defined as 'kitchen contact'; 'house contact'; and 'non-house contact'. In Thailand comparable levels were defined as 'house contact'; 'compound contact'; and 'neighbor contact'.

Results: In Bangladesh 1333, and in Thailand 129 new patients were included. The average new case detection rate over 10 yrs was 50 per 100,000 general population per year in Bangladesh, and 1.5 per 100,000 in Thailand. In the high endemic area 25% of newly detected cases were known to belong to a contact group and were not the index case of this group, whereas in the low endemic area 62% of newly detected cases had these characteristics. The distribution of the nearest index cases over the three contact levels was comparable in both areas. Just over half of the nearest index cases were found within the immediate family unit ('kitchen' in Bangladesh; 'house' in Thailand).

Conclusion: The results indicate that in a low endemic area a higher proportion of newly detected leprosy cases have a family history of leprosy compared to a high endemic area. Different contact levels and their relative risks to contract leprosy need to be established more precisely. In high endemic situations the circle of contacts that should be surveyed may need to be wider than currently practiced.

RÉSUMÉ

Contexte: Cet article est publié dans le cadre d'une étude plus large sur le rôle des contacts étroits dans la transmission de la lèpre. Elle s'est attachée à explorer si la proportion de nouveaux cas détectés dans une famille ayant un historique de lèpre diffère des taux variés d'incidence de lèpre dans une population.

Méthodes: Une analyse rétrospective fut entreprise sur les personnes au contact de tous les nouveaux cas diagnostiqués de lèpre, pendant une période de 10 ans au sein de programmes bien établis de contrôle de la lèpre en Thaïlande et au Bengladesh. Selon notre définition, un groupe contact consiste du nouveau cas accompagné des cas présents et passés qui étaient membre de la famille par naissance ou alliance. Pour un nouveau cas, le cas index le plus proche fut défini par le temps d'apparition des symptômes des cas dans le groupe

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contact, combiné à l'étroitesse de contact entre ces cas et le nouveau cas. Trois niveaux de contact furent distingués. Au Bengladesh, trois niveaux furent définis : les « contacts à la cuisine », les « contacts à la maison » et « les contacts hors maison ». En Thaïlande, des niveaux comparables furent définis comme « contact de la maison », « contact composite » et « contact de voisinage ».

Résultats: Au Bengladesh furent incorporés dans l'étude 1 333 nouveaux patients et en Thaïlande, 129. Le taux de détection moyen a été durant les dix années de 50 pour 100 000 personnes de la population générale et par an au Bengladesh, et de 1,5 pour 100 000 en Thaïlande. Dans la région hautement endémique, 25% des cas nouvellement détectés étaient connus comme appartenant à un groupe contact et ne furent pas le cas index pour ce groupe, tandis que dans la région faiblement endémique, 62% des cas nouvellement détectés avaient ces caractéristiques. La distribution des cas index les plus proches parmi les 3 niveaux de personnes contacts était comparable dans les deux régions. Un peu plus de la moitié des cas index fut trouvé dans l'unité familiale immédiate (la cuisine au Bengladesh et la maison en Thaïlande).

Conclusion: Ces résultats suggèrent que, dans une région faiblement endémique, la proportion de cas de lèpre nouvellement diagnostiquée ayant une histoire familiale de lèpre, est supérieure à celle rencontrée dans une région hautement endémique. Il sera important de plus précisément établir les niveaux de contact et leurs risques relatifs à contracter la lèpre. Dans les situations de haute endémicité, le cercle des contacts qui devrait être le sujet de surveillance épidémiologique devra être plus large que ce qui est couramment pratiqué.

RESUMEN

Panorama: Como parte de un estudio más extenso sobre el papel que juegan los contactos cercanos en la transmisión de *M. leprae*, en este estudio exploramos si la proporción de nuevos casos con historia familiar de lepra, difiere de la tasa de incidencia de lepra en la población general.

Métodos: Se hizo un análisis retrospectivo de contactos de todos los nuevos pacientes de lepra diagnosticados durante un periodo de 10 años en los programas de control de la lepra en Tailandia y Bangladesh. En nuestra definición, un grupo contacto consistió de los nuevos casos y de los casos pasados y presentes que fueron familiares y parientes de los nuevos casos. Para un nuevo caso, el caso índice más cercano se definió sobre la base del tiempo de aparición de los síntomas en los casos del grupo de contactos en combinación con el grado de contacto entre estos casos y el nuevo caso. Se definieron tres niveles comparables de contacto. En Bangladesh: "contactos de cocina," "contactos domésticos," y "contactos no domésticos"; en Tailandia: "contactos domésticos," "contactos compuestos" y "contactos vecinos."

Resultados: Se incluyeron 1333 nuevos casos en Bangladesh y 129 en Tailandia. La tasa promedio de detección de casos nuevos en 10 años fue de 50 por 100,000 por año en Bangladesh, y de 1.5 por 100,000 en Tailandia. En el área de alta endemia, el 25% de los nuevos casos detectados pertenecieron a un grupo de contactos y no fueron el caso índice en este grupo; en el área de baja endemia, el 62% de los nuevos casos detectados tuvieron estas características. La distribución de los casos índice más cercanos en los tres niveles de contacto fueron comparables en ambas áreas. Un poco más de la mitad de los casos índice más cercanos se encontraron dentro de la unidad familiar inmediata: "cocina" en Bangladesh, "domésticos" en Tailandia).

Conclusión: Los resultados indican que, en comparación con un área de alta endemia, en un área de baja endemia la mayor proporción de los nuevos casos detectados tienen una historia familiar de lepra. Se concluye que es necesario establecer con más precisión, los diferentes niveles de los contactos y sus riesgos relativos de contraer la enfermedad. En las situaciones de alta endemia también se requiere una vigilancia dentro del círculo de contactos, mayor que la que se realiza actualmente.

The importance of close contact with a leprosy patient in the transmission of *M. leprae* is well established. [2, 3, 5, 8] The relative risk for contracting leprosy is increased in people with contacts to leprosy patients in comparison to those in an endemic population without known contacts. The relative risk is higher for contacts of multibacillary (MB) leprosy patients than of paucibacillary (PB) patients. [2, 5, 13] Close contacts are

usually, but not necessarily, relatives living in the same house or compound. For this reason, leprosy control programs often conduct contact surveys when new leprosy cases are detected. By examining family and household members of a new case, there is a fair chance to find other cases of leprosy as well. But questions remains about the extent to which these contacts contribute to transmission of *M. leprae* in a community, and whether contact tracing and treatment contribute to interruption of transmission of the mycobacterium in that community.

Field workers and control program managers often suggest that with declining leprosy endemicity, the incidence in contacts of leprosy patients appears to decrease less rapidly than in the surrounding population. Apparently risk factors for the development of leprosy are distributed differently in contact groups of leprosy patients and the general population. The suggested change in the importance of contact however, has never been substantiated. Yet in order to design effective leprosy control measures, it is necessary to know the relative importance of (close) contacts in the total transmission of leprosy in different populations and the underlying mechanisms of this transmission. As part of a larger program studying the transmission of *M. leprae*, the objective of this study was to explore whether the proportion of newly detected cases known to be a close contact of a leprosy patient differs with different incidence rates of leprosy in a population. To this end, a high endemic area in Bangladesh is compared with a low endemic area in Thailand. All new patients during a certain period of time were investigated retrospectively with respect to the presence of leprosy patients (past and present) among relatives. In doing so, different levels of closeness of contact were distinguished. The findings of this exploration are intended to contribute to the interpretation of a prospective epidemiological study of the transmission of *M. leprae* and the role of close contacts therein. [7]

METHODS

Study area and leprosy control program

I. Bangladesh. The study was conducted in the subdistrict of Jaldhaka, a highly endemic area in Nilphamari District in northwest Bangladesh, with a population of approximately 250,000. The Danish-Bangladesh Leprosy Mission (DBLM) has been involved in leprosy control activities in this area since the late 1970's, and virtually all leprosy patients in the area are registered with DBLM. [9, 10] Jaldhaka was selected because of relatively good quality of contact surveys, which were conducted frequently by experienced staff. DBLM started contact surveillance in 1980 and this reached a good level of completeness by 1985. From 1987 onward, all persons sharing a kitchen with a newly detected case were to be examined once a year, for a period of 5 yrs in PB cases, and 10 yrs in MB cases. In 1994, the lengths of these periods were reduced to 2 and 5 yrs respectively. Active case finding also included school surveys, mass surveys and village checks. The study period was between 1987 and 1996 (10 yrs).

II. Thailand. The study was conducted in the Province of Chiang Mai in Northern Thailand. The following nine districts were selected: Chiang Mai city, Saraphi, Sansai, Doi Saket, Sankampaeng, Mae Rim, Mae Taeng, Hang Dong, and San Patong. The total population of the study area is approximately 850,000. Before the 1970's, almost all new leprosy cases in northern Thailand were detected by the McKean Rehabilitation Center in Chiang Mai, an institution of the Church of Christ in Thailand. With the integration of leprosy control in general health services, new cases in the area were also detected by the Leprosy Control Division of Northern Thailand or by Public Health Services since the 1970's. [12] Patient data were collected from both the McKean Rehabilitation Center and the Leprosy Control Division of Northern Thailand. The study districts were chosen because of the proximity to Chiang Mai city and good coverage of leprosy control activities in the past. These activities included health education, contact surveys, and school surveys. Contact surveys of new patients living in remote areas were not always performed in the house or village. These patients were advised to bring close relatives to the clinic for inspection on signs of leprosy. The study period was between 1988 and 1997 (10 yrs).

Definitions

Leprosy case definition. Leprosy control programs in both Bangladesh and Thailand adhered to the WHO definition for a leprosy case as 'a person showing clinical signs of leprosy, with or without bacteriological confirmation of the diagnosis, and requiring chemotherapy'. Following official guidelines, the program definitions for PB and MB changed several times in both countries during the study period. For consistency in data analysis, cases with Ridley Jopling classification BB, BL and LL and all cases with positive skin smears (BI >0) have in this study been defined as multibacillary (MB), and all other cases as paucibacillary (PB). All new leprosy cases who originated from the study area and who were detected during the study period were included in the study.

Definition of contact group and closeness of contact. For each new case, the group of patients that was considered consisted of the new case and of relatives and family-in-law. The relation of a patient from this contact group to the new case was in both study areas defined as: husband, wife, father, mother, son, daughter, brother, sister, grandparent, grandchild, uncle, aunt, nephew, niece, and cousin. There was also an 'other' category, in which other relationships could be specified, such as a stepparent or stepchild. Three contact levels were distinguished. In Bangladesh these levels were defined as 'kitchen contact' (the new case ate from the same kitchen as a given case from the contact group); 'house contact' (new case lived in the same house, but ate from a different kitchen: a house in this area of Bangladesh can have several kitchens); and 'non-house contact' (new case lived in a different house, possibly in another village or town). In Thailand comparable levels were defined as 'house contact' (the new case lived in the same house); 'compound contact' (new case lived in a separate house, but on the same compound); and 'neighbor contact' (new case lived in the same village or town, but not in the same compound). The contact level was taken to be that level of contact between the new case and a given case from the contact group at the time the given case was known to have leprosy. No time limit was set regarding the past duration of the contact.

Index definition. The index case of any group of cases with contact to one another was defined as the case with the earliest onset of symptoms, with time of onset calculated as registration date minus reported duration of symptoms at registration. In case of incomplete information, the registration date was used to determine the index case. For newly detected cases, the following procedure was adopted: First, it was determined whether the newly detected case was the index case of his/her contact group or not. If not, the index cases of the three closeness-of-contact circles around the newly detected case were determined, in widening order. Next, the nearest index case for a newly detected case was defined to be the first index case found, other than the new case him/herself. The procedure implies that the index case of the contact group and the nearest index case of the newly detected case were not necessarily the same case. The term 'index case' in this study does also not necessarily imply that this case was responsible for actual transmission. All individuals in a contact group might have been infected by other (possibly unknown) leprosy patients in the community.

Data collection and analysis

For each study area, a data collection form was developed in order to collect information not available in the existing patient databases. The additionally collected data included information on the new patients themselves (such as registration number, duration of symptoms, leprosy type and mode of detection) and information on contact related variables (such as contact status which indicates whether the new case belonged to a contact group or not, level of closeness of contact to the contact group members, registration numbers of the group members and relationships). The additional patient information was extracted from patient cards.

In Bangladesh, contact information on kitchen level was mainly extracted from contact surveillance cards. Information at house and non-house contact level was usually not recorded during contact surveillance, and information for identification of possible index cases at these levels was re-

TABLE 1.   *Distribution of new leprosy cases, for which the contact status was known, in Bangladesh and Thailand, by leprosy type, age and sex.*

	Study cases											
	Bangladesh						Thailand					
Sex	Male		Female		Total		Male		Female		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Leprosy type												
PB	608	82	388	86	996	83	25	38	9	26	34	34
MB	134	18	64	14	198	17	40	62	26	74	66	66
Unknown	2	0	1	0	3	0	0		0		0	
Age (in years)												
0–14	107	14	77	17	184	15	6	9	3	9	9	9
15–29	210	28	122	27	332	28	17	26	6	17	23	23
30–44	247	33	161	36	408	34	17	26	5	14	22	22
≥45	180	24	93	21	273	23	25	38	21	60	46	46
Total	744	100	453	100	1197	100	65	100	35	100	100	100

trieved from other sources with the help of the responsible leprosy control officers.

In Thailand information on contact surveys was incomplete. Therefore an additional effort was made to retrieve the necessary data from the patients themselves or immediate relatives through follow-up visits. In total 90 out of 129 (70%) eligible patients or their relatives were visited for the purpose of this study and the contact survey forms completed.

The primary objective of the study was to identify leprosy patients (past and present) who had had contact with the newly detected leprosy patients. Enumeration of all eligible contact group members was often impossible, especially outside the closest contact level considered (Bangladesh: kitchen; Thailand: house), because data were collected retrospectively and spanned a long period of time.

Data analysis was carried out with SPSS 7.0 for windows. Proportions were compared using the Chi-square test (p = 0.05).

RESULTS

In Jaldakha (Bangladesh), a total of 1333 new patients were detected between 1987 and 1996. The contact status was known for 1197 patients (90% of the included population). For these patients the distribution of leprosy type, age by sex is given in Table 1. Of the 1197 cases, 744 (62%) were male

and 453 (38%) female, giving a male:female ratio of 1.6:1. There were 996 PB cases (83%) and 198 MB cases (17%). In 3 cases the leprosy type was unknown. The average new case detection rate over the period was 50 per 100,000 general population per year.

In Chiang Mai (Thailand) a total of 129 new cases were detected between 1988 and 1997. Of these, the contact status was known for 100 patients (78% of the included population). The distribution of leprosy type, age by sex for these patients is given in Table 1. Of these, 65 (65%) were male and 35 (35%) female, giving a male:female ratio of 1.9:1. There were 34 PB cases (34%) and 66 MB cases (66%). The average new case detection rate over the period was 1.5 per 100,000 general population per year.

In Bangladesh, the overall percentage of newly detected cases with a known index case was 25% only (Table 2). The percentage was highest in the youngest age group of 0–14 yrs (48%), and decreased to 28% in the age group 15–26 yrs, and 19% and 16% in the age groups 30–44 and 3 45 yrs respectively. In the remaining cases (75%), no leprosy patients were found within the three defined contact levels. Also included in Table 2 is the distribution of the nearest index cases over the three levels of closeness of contact for the newly detected pa-

TABLE 2. *Status of newly detected cases (by age) in Bangladesh and Thailand, according to closeness of family contact to the nearest index case.*

	Age (in years)								Total	
	0–14		15–29		30–44		≥45			
Bangladesh	n	%	n	%	n	%	n	%	n	%
Contact to										
known index	88	48	92	28	76	19	44	16	300	25
Kitchen contact	60	68	47	51	32	42	19	43	158	53
House contact	16	18	29	32	24	32	8	18	77	26
Non-house contact	12	14	16	17	20	26	17	39	65	22
No contact to										
known index	96	52	240	72	332	81	229	84	897	75
Total	184	100	332	100	408	100	273	100	1197	100
Thailand	n	%	n	%	n	%	n	%	n	%
Contact to										
known index	6	67	18	78	14	64	24	52	62	62
House contact	6	100	10	56	11	79	10	42	37	60
Compound contact	0	0	6	33	3	21	7	29	16	26
Neighbor contact	0	0	2	11	0	0	7	29	9	14
No contact to										
known index	3	22	5	22	8	36	22	48	38	38
Total	9	100	23	100	22	100	46	100	100	100

tients with known positive family history. The nearest index cases were found at kitchen level in 53% of the cases. The percentage of kitchen contact was highest in the youngest age group (68%), and decreased to 51% in the age group 15–29 yrs, and to 42% and 43% in the age groups 30–44 and ≥45 yrs respectively.

In Thailand, the overall percentage of newly detected cases with a known index case was as high as 62% (Table 2). The percentage was highest in the age groups 0–14 yrs (67%) and 15–29 (78%), and decreased slightly to 64% and 52% in the age groups 30–44 and ≥45 yrs respectively. In the remaining cases (38%), no leprosy cases were found within the three defined contact levels. In cases with known positive family history, the nearest index cases were found at house level in 60% of the cases. The percentage of house contact was highest in the youngest age group (100%), and decreased to 56% in the age group 15–29 yrs, to 79% in the age group 30–44 yrs, and to 42% in the group 45 yrs and older.

The difference in percentage of newly detected leprosy cases with contact to a known index case between Bangladesh (overall 25%) and Thailand (overall 62%) is statistically significant (Chi-square test: $p < 0.05$).

DISCUSSION

The objective of this study was to explore whether the proportion of newly detected leprosy cases with a family history of leprosy is higher in a population with a lower incidence rate of leprosy. To this end, a retrospective study was undertaken in two areas; northwest Bangladesh with a high new case detection rate of approximately 50 per 100,000 per year, and northern Thailand with a low new case detection rate of approximately 1.5 per 100,000 per year. This study shows that in the chosen high endemic area approximately only 25% of newly detected cases have a known index case within the family, whereas in the chosen low endemic area this proportion is as high as 62%. The distribution of nearest index cases over three different contact levels was comparable in both areas. Just over half of the nearest index cases are found within the immediate family unit (kitchen in Bangladesh; house in Thailand). In Bangladesh, children aged 0–14 yrs most often have known index cases among rela-

tives, with the nearest index primarily within the immediate family unit. The proportion with a known index case decreases over the age groups. Although less marked, in Thailand there is also a difference over the age groups. However, there is an important difference in age distribution of the newly diagnosed patients in both countries, with a higher average age in Thailand. This is probably a reflection of the level of transmission. In Thailand transmission has been low in the past two decades, and many new patients are likely to have been infected in the past and have had long incubation periods. Increasing average age of newly detected patients with the decline of leprosy incidence has been described previously. [1,4]

Obviously, there are many limitations to direct comparisons between countries. There are geographical, socio-economic and cultural differences, as well as differences with regard to the provision of health services in general and leprosy control in particular. All these differences will have effect on transmission patterns and the detection of leprosy. An important difference, for instance, between the countries is the proportion of MB patients. In Bangladesh this is approximately 20%, while in Thailand over 60% are MB. Such differences between countries have been observed before, and are possibly explained by genetic differences. [1] With a higher proportion of patients with MB leprosy, one might expect transmission of *M. leprae* in the population to be more intensive, resulting in a higher endemic level of leprosy. However, this is not consistent with our findings of proportion of MB and the leprosy incidence in the two populations studied, which perhaps might be due to a difference between the individuals in these populations with respect to susceptibility to developing leprosy.

There are also important limitations in the methodology of the study. It is a retrospective analysis of routine data. The exact number of family members with past or present leprosy at the beginning of the observation period, or developing leprosy during this period, could not be established prospectively. Also denominator data, the total number of eligible family members within the defined contact levels per newly detected patient, are absent. Denominator information, however, is not strictly neces-

sary when establishing the presence of family members with past or present leprosy for a newly detected patient. There are differences in average size of the contact groups between the countries, with households in Bangladesh tending to be larger and thus theoretically with a higher chance of leprosy cases in households. This difference in fact strengthens our findings. Lack of denominator information makes interpretation of relative risks for developing leprosy in and outside leprosy contact groups less straightforward, but this kind of calculation was outside the scope of the study. Finally, case detection efforts were more intensive at the closest contact level (Bangladesh: kitchen; Thailand: house) compared to the other levels, leading to a possible underestimation of numbers of cases at these other levels. While taking these limitations into account, we believe that the very large difference in newly detected leprosy patients with a known index case between both areas represents a valid observation regarding this proportion in different endemic situations. Differences in the leprosy control program and data collection between the two areas alone would not lead to such great difference in outcome (25% versus 62%), suggesting a genuine difference between the areas. However, the exact extent of the difference can only be established if adjustment for these factors would be possible.

The implications of our findings for transmission of *M. leprae* in general are important, but not easily interpreted. It is likely that in a high endemic area such as northwest Bangladesh, most transmission in the population occurs outside close contacts of known leprosy patients. Up to 75% of new patients in Jaldakha district did not have any known index case. But the contact definition used in this study was strict, consisting of (close) relatives only. In a retrospective study over 25 yrs in a high endemic village of 2283 inhabitants in Sulawesi, Indonesia, it was shown that new patients could also be linked to previous cases other than from their own household. Besides household index cases in 28% of new cases, there were first neighbor cases in 24%; second neighbor cases in 12%; cases within the social network in 10%; and cases among relatives living elsewhere in

5% of the new cases. Thus 79% of all new cases could be linked to an index case. [14] Leprosy cases are not distributed evenly among the population, but are known to cluster. Our observation of a high percentage of relatives with leprosy in Thailand compared to Bangladesh supports the hypothesis that the relative importance of clustering becomes stronger with declining endemicity of leprosy in a population.

The challenge for leprosy control is to determine which contact levels need to be surveyed in order to significantly interrupt transmission of *M. leprae* in the population. In order to do so, it appears that in high endemic situations, apart from early case finding, the circle of contacts to be surveyed needs to be wider than currently practiced. Also, the different contact levels and their relative risks to contract leprosy need to be defined more precisely. Lessons can possibly be learned from tuberculosis control, where contact tracing is performed according to the 'stone-in-the-pond' principle.[6, 15] If the prevalence of tuberculosis within close proximity of a new case exceeds an expected level, the survey is extended to a next, wider range of contacts. This approach is continued until the prevalence of tuberculosis cases in the expanding circle of contacts reaches the prevalence level of the general population. The finding in Thailand that the nearest index case is most often found in very close proximity to the patient could indicate that with declining incidence of leprosy, the extent of contact surveys could be reduced.

From a methodological point of view this study represents only a limited attempt to gain insight in the epidemiology of contact transmission. Further research, preferably prospective and with precise definitions of contact levels, is needed to understand the role of contact in leprosy under various endemic circumstances, underlying patterns of transmission, and implications for leprosy control. The effect of interventions targeting contacts such as chemoprophylaxis, on the overall transmission of *M. leprae* in a population also needs clarification.[11] Such a study is currently underway in Bangladesh.[7] The application of advanced techniques of epidemiological modeling is invaluable to help analyze and interpret existing and new data in this area. The result of the present study is just one step towards this end.

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