Delay in Leprosy Diagnosis — A multi-center, multi-country Asian study

Erik Post^a, Wim Brandsma^b, Inge Wagenaar^c, Khorshed Alam^{d, †}, Vanaja Shetty^{e, †}, Sajid Husain^{f, †}, Cita Rosita Sigit Prakoeswa^{g, †}, Mahesh Shah^{h, †} & Krishna Bahadur Tamang^{i, †}

^a*For Tenlepe study: Sr. Advisor Health, Royal Tropical Institute, Amsterdam, The Netherlands*

^b*Retired, consultant, Leprosy - Hand Rehabilitation, Green Pastures Hospital and Rehabilitation Center, International Nepal Fellowship, P.O. Box 5, Pokhara, Nepal*

^c*Centre for Infectious Disease Control, National Institute of Public Health, and the Environment (RIVM), Bilthoven, The Netherlands*

^d*Rural Health Program, The Leprosy Mission International Bangladesh, Nilphamari, Bangladesh*

^e*Foundation for Medical Research, Mumbai, India*

^f*JALMA Institute of Leprosy & Other Mycobacterial Diseases, Agra, India*

^g*Dr. Soetomo Teaching Hospital—Universitas Airlangga, Surabaya, Indonesia*

^h*Anandaban Hospital and Mycobacterial Research Laboratories, The Leprosy Mission Nepal, Kathmandu, Nepal*

ⁱ*Lalgadh Leprosy Hospital and Services Centre Dhanusha, Lalgadh, Nepal*

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Summary Delay in reporting for possible leprosy diagnosis and a delay in making the diagnosis of leprosy may result in unnecessary complications.

Objective: Which factors contribute to late reporting and a missed diagnosis of leprosy?

Method: A questionnaire, involving 1243 newly diagnosed patients, was used to explore reasons for possible delay in diagnosis and start of treatment; the patients were being managed in six projects in four leprosy endemic countries, and needed treatment for nerve function impairment,

Results/Conclusions: Delays in reporting for diagnosis and in establishing the diagnosis are multifactorial and differ between the research sites. Factors contributing to the delay are person and program related, including concealment of suspected disease, perhaps because of shame, accessibility of the clinic, and expertise within the

Correspondence to: W. Brandsma (e-mail: jwbrandsma@gmail.com)

[†] Study sites Principle Investigator.

diagnostic services. They need to be addressed in different ways to minimize delay thereby reducing risks for complications.

Keywords: Epidemiology, stigma, delay in diagnosis

Introduction

Leprosy is a bacterial infectious disease nowadays only endemic in (sub)tropical countries. The global annual incidence is approximately 220,000 patients. The disease is most prevalent in a few Asian and African countries and Brazil¹ where it mostly affects people in economically less advanced, rural, areas.

Timely diagnosis and adequate treatment and follow up can, to a large extent, prevent immunologically and treatment-induced complications, in particular, damage to the peripheral nerves known as neuropathy. Often, the diagnosis is delayed, and many patients first report with neuropathy. However, neuropathy and other complications may also develop following diagnosis and even after completion of treatment.² The shorter the delay, the less likely that patients may develop complications.

Multiple studies from endemic areas have reported on the delay in diagnosis and the detrimental effects that this can have on patients and the community: Paragua;³ Bangladesh,⁴ Nepal;⁵ Ethiopia,⁶ Nigeria,^{7–9} Brazil,^{10, 11} and China.¹²

These effects relate to continued transmission of the disease through untreated infectious patients and the effect that progression of untreated leprosy can have on the infected individuals, including progressive neuropathy and the development of new impairments.

Delay in diagnosis has also been reported from nonendemic countries where leprosy can be considered an imported disease: Denmark,¹³ United Kingdom,¹⁴ and USA.¹⁵

Insight into reasons for delay may help to develop specific messages and actions to raise awareness about the disease, which may then result in earlier reporting for diagnosis, and adequate treatment.^{16, 17}

Methods

This study of delay in reporting was part of two parallel trials assessing the efficacy of corticosteroids in the prevention (subclinical trial) or treatment (clinical trial) of nerve function impairment (NFI).¹⁸

Newly diagnosed leprosy patients, between the ages of 15 and 60, with electro-neurophysiologically confirmed NFI (subclinical trial) and patients with clinical NFI, were enrolled in the study.

At the time of inclusion, a semistructured questionnaire was used by the medical doctor, social worker, or senior leprosy field worker (Appendix A). All were trained in administering the questionnaire. Patients were asked about the time between first symptoms and actual diagnosis, what actions had been taken and who was informed about the disease. In this study, delay was defined as the time between the onset of first symptoms related to leprosy, and a correct medical diagnosis. In some centers, patients were mostly included from a 'base' hospital, in others from a field leprosy program. Patients were included as they reported to a program for diagnosis.

Six leprosy centers in four leprosy endemic countries in Asia participated in the trials: Indonesia, Bangladesh, India (2) and Nepal (2). Inclusion of patients was from April 2012–April 2014.

Table 1. Enrollment in both trials

Center	Subclinical trial	Clinical trial	Interviewed (%) about 'delay'
Bangladesh	118	235	100
India—A	67	82	100
India—B	137	231	99.7
Nepal—A	48	166	100
Nepal—B	*	55	100
Indonesia	*	104	94.2
	370	873	1243

Centers * did not participate in subclinical trials.

Table 2. Reported delay in months (range) between first symptoms and reporting for diagnosis

Center	N	Subclinical NFI trial	N	Clinical NFI trial
Bangladesh		12 (6–24)		8 (4–18)
Male	65	12 (6–24)	183	9 (4–18)
Female	53	12 (6–24)	52	7 (5–13.5)
India—A		14 (9–36)		12 (5–48)
Male	52	18 (8.5–36)	70	12 (5–48)
Female	15	12 (8–13.5)	12	6.5 (6–37)
India—B		2 (2–3)		3 (2–3)
Male	117	2 (2–3)	191	3 (2–3)
Female	20	2 (2–3)	40	3 (2–3)
Nepal—A		6.5 (3–12)		5 (2–12)
Male	42	6 (3–12)	121	5 (2–12)
Female	7	12 (8–12)	51	5 (3–6)
Nepal—B*	—			12 (5–24)
Male			40	12 (5–24)
Female			15	7 (3–15.5)
Indonesia*	—			7 (4–12)
Male			72	9 (5–12)
Female			23	5 (2.5–11)

Center * did not participate in subclinical trial (No equipment to assess subclinical) neurophysiologically NFI.

Data were entered locally and sent from the various centers through the Internet service 'Drop Box' to the statistician. Only the statistician and the three primary authors had access to the centers' combined data. Ethical approval was obtained from all national ethics committees and the participating centers. All patients gave their informed consent.

Results

The total enrollment in both trials was 1243 patients. Table 1 shows enrollment by center for each of the two studies and the percentage of delay questionnaires completed.

Table 2 gives the time of patients' delay in reporting for diagnosis based on recall of first signs and/or symptoms. A wide difference can be seen between centers within a given country and between countries, in particular between the two centers in India, and the two in Nepal; we do not have an obvious explanation for this. A difference in delay between male and female patients reporting late for diagnosis is also noticeable.

The reasons for delay were many and are summarized for one center in Table 3 (see Discussion).

Table 3. Reasons for delay*

Center: Nepal—A	Men	Women
Not aware/did not recognize	18	11
Failure to diagnose by MD	7	1
Negligence	6	0
Other/no reason	6	3
No delay	3	0
Total	40	15

Table 4. First sign/symptom as recalled by patients (%)

	Skin lesion (Pale)		Skin lesions (Red)		Anesthesia	
	Subclinical trial	Clinical trial	Subclinical trial	Clinical trial	Subclinical trial	Clinical trial
Bangladesh	85	46	0	0	9	25
India—A	46	30	29	0	0	29
India—B	67	32	0	0	26	55
Nepal—A	39	39	35	0	0	28
Nepal—B*	—	22	—	22	—	—
Indonesia*	—	34	—	26	—	—

Center * did not participate in subclinical trial.

Table 5. Recognizing the possibility of leprosy (%)

Center	Subclinical trial (%)	Clinical trial (%)
Bangladesh	17	20
India—A	3	3
India—B	0	0
Nepal—A	0	<1
Nepal—B*	—	7
Indonesia*	—	14

Center * did not participate in subclinical trial.

What sign/symptom triggered the visit to a health worker? Was it a skin lesion or loss of sensation (anesthesia)? The first sign/symptom as recalled by patients is given in Table 4.

The patients were asked if they recognized the possibility of leprosy when they had noticed the first signs/symptoms (Table 5). An important question that reflects the extent to which people are aware of the possibility of leprosy and feel free to disclose or conceal the diagnosis.

Discussion

This study has shown that delay in diagnosis, and thus treatment, is a major problem for all countries/research sites where the study took place. There is a notable exception in one of the centers where the median delay was reported as 2 and 3 months in the subclinical and clinical trials, respectively (Table 2).

Early diagnosis of the disease is important for two main reasons:

It may prevent the onset of immunologically induced neurological complications that may lead to irreversible nerve damage and ‘disability’. Secondly, from a community health

and disease prevention point of view, the earlier the diagnosis, the smaller the window of transmission by those patients who are discharging bacilli into the environment.

Many of the questions required the patients to recall certain timepoints, such as the timing of the first symptom, when the possibility of leprosy was first considered, or the first place of contact for help. When symptoms initially are mild and may have been present for many months or even years, there will be recall bias. Nevertheless, the tables clearly show considerable delay.

To achieve early diagnosis, a two-pronged approach is needed: community awareness/education that does convey the right information and facts about disease recognition and treatment. This would also address fear, shame, and anxiety that often still prevail and often are a reason for delay in reporting. Second, education of health staff in leprosy endemic countries to 'think leprosy' and know at least of the main cardinal sign and how to test for this.

The study showed that very few patients considered the possibility of leprosy when first symptoms appeared (Table 5). The highest reported percentage was 20% in one research site. This points to the importance of public and medical education in reporting and recognition of early signs and symptoms.

Table 3 states multiple reasons for delay for one center. Most centers 'struggled' with this open question and answers were not particularly useful for analysis. One center consistently answered 'Ignorance'.

A systematic review related to delay in presentation and delay in the diagnosis and treatment of tuberculosis classified risk factors in sociopsychological, sociodemographic, and socioeconomic areas.¹⁹

Table 4 shows the differences in recording first sign of leprosy i.e. pale or red skin lesion(s) or anesthesia. The table shows distinct differences between study sites and trials for which we do not have an explanation. Differences between staff expertise, workload, and communication issues may all have contributed to these differences.

We believe that a questionnaire, such as used in the TENLEP study, provides information that is useful for personalized 'education'. Aggregated data from a center or leprosy control program will give insight in cultural attitudes and behavior that should be addressed to facilitate the early reporting and diagnosis of leprosy.^{16, 17}

There are multiple patient/community and health system related factors that determine early reporting and diagnosis. These factors need systematic surveying and assessing and should be addressed in culturally meaningful and sensitive ways.^{20, 21}

Limitations/strengths: 'Delay' questionnaires were completed for most patients (Table 1). However, many questionnaires were incomplete and/or questions were ill-understood or, when an open question such as 'What does the patient say was the main reason for delay in diagnosis' was asked, were just answered by 'ignorance'. The delay study was piggybacking on a much larger study which involved multiple clinical examinations which may have led to suboptimal 'input' from interviewer and interviewee regarding the 'delay' questionnaire.

Also, with available data it was difficult to analyze possible differences between patient delay and health system delay i.e., patients reporting with leprosy signs, but correct diagnosis not made by the health staff.

The main objective of the study was to investigate the effectiveness/efficacy of prednisolone in the prevention and treatment of NFI. We strongly feel that outcomes for the 'delay' study was influenced by participants commitment and focused primarily on the primary outcomes of the main studies. An additional questionnaire was often seen as needing extra time. Little time was then often taken to explore beyond the 'obvious' answers.

A major strength of the study is that it has been using a standard semistructured questionnaire across six different projects showing differences in outcome regarding reasons and factors for delay. The social consequences, also part of the questionnaire, will be analyzed and reported in a separate paper.

KEY POINTS AND RECOMMENDATIONS:

- Delay in reporting for diagnosis and treatment is an important contributing factor in the onset of neuropathy.
- The study shows that (reasons for) delay in reporting/diagnosis are many and vary between leprosy endemic areas.
- Reasons for delay need to be addressed with appropriate culturally sensitive methods.

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Appendix A. TENLEP Form 4—Reasons for delay in presentation and start of treatment

Collect the data required here through interviewing the patient. Do NOT do this at time of diagnosis or enrollment to the Trials but at time of first or second return visit.

TENLEP Trial Form 4	Part One— Patient ID and visit date
Patient TENLEP ID Number:	
Week Number: <i>Enter as week number, 4, 8 or 12 as appropriate.</i>	
Visit date: <i>dd-mm-yyyy</i>	_/_/_
Hospital/Clinic Record Card Number:	
Assessed by: <i>Enter staff name</i>	

TENLEP Trial Form 4	Part Two – Patient reported delay in diagnosis
Ask the patient how many months it is since he/she became aware of the first sign or symptom of leprosy <i>Record as number of months</i>	

TENLEP Trial Form 4**Part Three – Patient's symptoms & help-seeking**

Interviewer – Please ask the patient to tell you about all the times and places he/she went to seek advice, help, diagnosis or treatment. When you have a clear idea of the symptoms, actions taken to seek help and the length of delay, please ask the patient to answer the following questions.

What was the patient's first symptom of leprosy? Enter one number only from the list: <div style="display: flex; justify-content: space-between;"> <div> 1. Pale skin lesion(s), 2. Red skin lesion(s), 3. Anaesthesia 4. Loss of warm sensation 5. Burning/Tingling </div> <div> 6. Loss of muscle strength, 7. Symptom of Type1 reaction 8. Symptom of Type 2 reaction 9. Other (Specify) </div> </div>		<div style="border-bottom: 1px solid black; height: 1.2em; width: 100%;"></div> <div style="border-bottom: 1px solid black; height: 1.2em; width: 100%;"></div>
At that time did the patient recognise the possibility of leprosy? Yes/No/Don't know		
Where was the first place the patient went to get help? <div style="display: flex;"> <div style="flex: 1;"> 1. Go to pharmacist 2. Go to traditional healer 3. Go to alternative medicine practitioner 4. Go to private or health service clinic/doctor 5. Leprosy hospital or clinic 6. Person affected by leprosy 7. Other - specify </div> <div style="flex: 1;"> <div style="border-bottom: 1px solid black; height: 1.2em; width: 100%;"></div> <div style="border-bottom: 1px solid black; height: 1.2em; width: 100%;"></div> </div> </div>		
Who was involved in decision-making? <div style="display: flex;"> <div style="flex: 1;"> 1. Alone 2. Spouse 3. Jointly with spouse 4. Other family member 5. PAL 6. Other - specify </div> <div style="flex: 1;"></div> </div>		
Did the patient ever have MDT prescribed in the past but he/she did not completed the treatment? Yes/No/Don't know		
If "Yes", how many months of treatment were completed?		
What does the patient say was the main reason for delay in diagnosis and start of treatment? (Unlimited multi-line space for data entry)	<div style="border-bottom: 1px solid black; height: 1.2em; width: 100%;"></div> <div style="border-bottom: 1px solid black; height: 1.2em; width: 100%;"></div>	

TENLEP Trial Form 4		Part Four – Problems associated with leprosy					
Telling people about the leprosy diagnosis		Spouse	Family	Education/ Work	Friends	Neighbours	Community
Who already knows? <i>Tick those that apply</i>							
Who else will the patient tell? <i>Tick those that apply</i>							
Who does the patient NOT want to know? <i>Tick those that apply</i>							
Problems in relationships caused by the leprosy diagnosis		In marriage or marriage	With family members	In education or work	With friends	With neighbours	With community
Has it already caused a problem? <i>Tick those that apply</i>							
May it cause a problem in the future? <i>Tick those that apply</i>							

TENLEP Trial Form 4		Part Five – Revised estimate of delay	
Interviewer's estimate of time since first symptom (months)? <i>May be the same, less or more than that reported by the patient</i>			