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Epidemiological Characteristics of Leprosy Reactions: 15 Years Experience from North India[1]

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ABSTRACT

A retrospective analysis of patient's leprosy clinic records at PGIMER, Chandigarh, India for the period 1983 to 1998 was undertaken to study the frequency, time of onset, and risk factors for leprosy reactions. Of the 2600 cases analyzed, 1494 were multibacillary and 1106 had paucibacillary disease. Presentation with reaction was common with 30.9% of our patients having reactions at the time of first visit. The incidence of reversal reaction (RR) was highest during 6 to 12 months after starting multi-drug therapy (MDT), thereafter declining gradually. Late RR occurred in 9.5% of all cases and was noted up to 7 years after treatment. Female gender, widespread disease, and multibacillary disease were identified as risk factors for RR. Erythema nodosum leprosum (ENL) reactions were noted to occur mostly during second or third year after starting MDT. Of the total number of patients who experienced ENL, 64.3% had recurrent episodes which continued for up to 8 years after the start of treatment. Lepromatous leprosy, female gender, and high Bacterial Index (≥3) were recognized as risk factors for developing ENL. Occurrence of recurrent and late reactions, even though of mild severity, highlights the importance of recognizing and treating them promptly to prevent or reduce morbidity, complications, and further deterioration in the disability status. Although it is hoped that leprosy will have been eliminated at all levels by 2005, the recognition and management of these reactions will continue to be the most essential/significant task in the post elimination era.

RÉSUMÉ

Une analyse rétrospective des dossiers cliniques de patients traités à la clinique contre la lèpre du PGIMER de Chandigarh aux Indes fut conduite de 1983 à 1998, afin d'étudier la fréquence, la date d'apparition et les facteurs de risque des réactions lépreuses. Parmi les 2600 cas analysés, 1494 souffraient de maladie multibacillaires et 1106 de maladie paucibacillaire. Les réactions étaient fréquentes au moment de la première visite, étant de 30,9%. L'incidence de réactions reverses (RR) fut la plus élevée pendant les 6 à 12 mois suivant le début de la polychimiothérapie (PCT), puis déclinèrent graduellement. Des RR tardives apparurent dans 9,5% du nombre total de cas et furent détectées jusqu'à 7 années après traitement. Le sexe féminin, maladie disséminée et maladie multibacillaires furent

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identifiés comme des facteurs de risques de la RR. L'érythème noueux lépreux (ENL) fut principalement détecté durant les deuxième et troisième années après le début de la PCT. Parmi les patients ayant déclarés un ENL, 64,3% ont souffert d'épisodes cliniques récurrents et ce, pendant parfois plus de 8 années après le début du traitement. Une lèpre lépromateuse, un sexe féminin et un index bactérioscopique élevé (≥3) furent identifiés comme des facteurs de risque pour le développement d'un ENL. La survenue de réactions récurrentes ou tardives, même si elles sont de faible sévérité, souligne l'importance de les reconnaître et de les traiter rapidement afin de prévenir ou réduire la morbidité, les complications et une plus grande détérioration de l'état de handicap. Cependant, l'espoir de voir la lèpre éliminée à tous les niveaux vers 2005 est terni par l'enjeu essentiel, qui se devra d'être significatif, de reconnaître et de traiter ces réactions dans l'ère de l'après éradication.

RESUMEN

Se realizó un estudio retrospectivo de los expedientes clínicos de los pacientes con lepra en el PGIMER de Chandigarh, India, del periodo 1983 a 1998, para analizar la frecuencia, el tiempo de aparición, y los factores de riesgo de las reacciones leprosas (RL). De los 2600 casos analizados, 1494 fueron multibacilares y 1106 paucibacilares. La presencia de reacción leprosa fue común; 30.9% de los pacientes tuvieron RL en el tiempo de su primera visita. La incidencia de reacción reversa (RR) fue más alta entre los 6 y 12 meses después de haber iniciado el tratamiento con poliquimioterapia (PQT) y después declinó gradualmente. La RR tardía ocurrió en el 9.5% de todos los casos y se observó hasta 7 años después del tratamiento. El género femenino, la enfermedad diseminada y la enfermedad bacilar, se identificaron como factores de riesgo para la RR. Las reacciones tipo eritema nudoso leproso (ENL) se observaron más frecuentemente durante el segundo y tercer año del inicio de la PQT. Del total de los pacientes que desarrollaron ENL, el 64.3% tuvieron episodios recurrentes que continuaron hasta 8 años después de haber iniciado el tratamiento. La enfermedad lepromatosa, el género femenino y los IB altos (≥3) se reconocieron como factores de riesgo para el ENL. La ocurrencia de las reacciones recurrentes y tardías, aunque sean de severidad moderada, subraya la importancia de reconocerlas y tratarlas prontamente para prevenir o para reducir la morbilidad, las complicaciones y el progreso de las deformidades incapacitantes. Aunque se espera que la lepra se haya podido eliminar en todos sus niveles hacia el año 2005, el reconocimiento y manejo de las reacciones leprosas continuará siendo el reto más importante y esencial en la era de la post-eliminación de la enfermedad.

With the success of multi-drug therapy (MDT) in the treatment of leprosy, attention has focused on the problem of leprosy reactions, which are now the most significant issue in the management of individual patients. Despite a large burden of leprosy cases in India, very limited data has been published on the epidemiology of reactions from this part of the world. The available information about the epidemiology of leprosy reactions is incomplete and scanty, despite a growing amount of literature on its treatment.

Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, is a tertiary care institute in Northern India, which is a low endemic area for leprosy. Many patients with leprosy are self-referred and some are referred by a doctor or clinic, citing the better quality of care available at our center. In addition to the population of this region, the institute also caters to a large migrant population from various states of the country where leprosy is endemic. In the leprosy clinic at the institute, a good record keeping system combined with regular evaluation of patients has generated a very large and useful database for retrospective analysis of reactions in leprosy. Systematic analysis of these records was carried out to determine the incidence of leprosy reactions in our patients, and to identify risk factors if any. In this paper, we discuss the incidence and risk factors for leprosy reactions over the last 15 years.

MATERIALS AND METHODS

A total of 2867 new, previously untreated patients enrolled in the leprosy clinic at PGIMER during the period from 1983 to 1998 were included in the study. Patients with pure neuritic leprosy were excluded from this analysis. Until 1987 all patients with Bacterial Index (BI) ≥2 were classified

as multibacillary (MB), and <2 as paucibacillary (PB). From 1988 to 1998, all patients having positive slit skin smear were assigned to the MB group. Until 1994, all MB cases were treated with WHO MDT MB regimen for a minimum period of 2 yrs or until skin smear negativity, whichever occurred last. From 1994 to 1998, they were treated with fixed duration (24 months) MDT MB regimen.

After release from treatment (RFT), patients were seen at intervals of 3 to 6 months for the initial 2 years and later once or twice a year. Apart from this, patients were instructed on features of reactions/relapse, and told to attend the clinic immediately if they ever experience such symptoms or any other problems. A detailed clinical examination was done on each visit and skin smears are taken at least once a year. Details about time of onset and clinical features of reactions are recorded in the patient's record file.

Reversal reaction (RR) involving skin was diagnosed if the patient had redness and swelling of (already existing) lesions, or the appearance of a few new lesions close to the existing lesions or at distant sites, with or without tenderness of lesions. Neuritis as a part of reaction was defined as spontaneous pain (shooting, tingling, or burning), or tenderness of the nerves with nerve function impairment (NFI). In most patients with reactions, features of concomitant skin and nerve involvement were present. Erythema nodosum leprosum (ENL) was diagnosed if a patient developed multiple, usually small, tender, evanescent nodules, with or without ulceration, which were usually associated with constitutional symptoms. Wherever indicated, reactional episodes were treated with oral prednisolone (40–60 mg/day) tapered to a stop over 12 weeks. Occurrence of a RR after six months of stopping MDT was labeled as late RR. Recurrent episodes of RR or ENL were defined as having a recurrence of symptoms of either type of reaction more than six weeks after the completion of treatment for reaction. Recurrence of a reactional episode earlier than this was considered to be possibly due to inadequate or abrupt stoppage of treatment. The exact definitions of the spectrum of the disease and duration of treatment with MDT were not uniform in all the patients due to changing definitions of PB/MB cases by the WHO; however, from a purely academic/research point of view we have also tried to analyze trends of reactional events at presentation, during MDT, and after release from treatment, according to Ridley Jopling classification ([5]) among subgroups of PB/MB cases. For validation of our supposition and better understanding, we have used certain terminologies like "disseminated disease" and "late ENL" because of the absence (or not very satisfactory) definitions about reactions. Patients were labelled as having "disseminated disease," if there were ≥3 body areas involved, 6 or more skin lesions, or involvement of at least 2 peripheral nerve trunks. We have used the terminology "late ENL" for occurrence of ENL reaction 2 years after MDT completion.

The chi square test was used to analyze the difference between proportions and to identify trends. The difference between two unpaired sample means was tested using the student's *t*-test. The significance of various risk factors for developing reactions was analyzed with Cox's proportional hazards regression, and the results were expressed as rate ratios. Of the ratio, the 95% confidence interval is given.

RESULTS

Patients. Out of these 2867 patients, 62 patients were excluded, either because the diagnosis was changed or records were not complete. Another 205 patients were lost to follow-up or left the area after diagnosis. A total of 2600 patients with follow-up available up to 13 yrs (at least 3 yrs) were eligible for analysis. Average period of follow-up was 74 months (range 36 to 156 months). There were 1634 males (mean age 36 ± 3.2 yrs) and 966 females (mean age 39 ± 2.3 yrs). Out of them, 1494 (57.5%) had MB and 1106 (42.5%) had PB disease.

Incidence. The incidence of reversal reactions (RR) and erythema nodosum leprosum (ENL), and their distribution in PB/MB cases at the time of first presentation to the clinic is given in Table 1. The incidence of RR was 24.1% (627/2600 patients) and the figure for ENL in MB cases was 11.8% (177/1494 patients). Of the 627 patients with RR, 169 (27%) had evidence of reaction in skin lesions only and the re-

TABLE 1. *Prevalence of reactions at the time of first presentation.*

Classification	No. of cases	Reversal reaction			ENL		
		Skin only	Skin + nerves	Total (%)	Skin only	Skin + nerves	Total (%)
MB	1494	108	291	399 (26.7)	86	91	177 (11.8)
PB	1106	61	167	228 (20.6)	0	0	0
Total	2600	169	458	627 (24.1)	86	91	177 (11.8)

maining 458 (73%) had involvement of both skin and nerves, whereas in patients having ENL, 86 (48.6%) had only cutaneous involvement and 91 (51.4%) had involvement of both skin and nerves.

In the total period of observation, 858 patients experienced RRs and 337/1494 MB cases had ENL either at the time of registration, during, or after release from treatment with cumulative incidence of 33% and 22.5%, respectively. Altogether, there were 1356 episodes of RR in 858 patients (1.6 reaction episodes/patient) and 885 episodes of ENL in 337 patients (2.6 reaction episodes/patient). Of these 337 MB cases, 203 were treated before 1994 and the rest received fixed duration (24 months) MDT ($p < 0.05$).

Time of onset. Figures about the reactional episodes according to the period of time they occurred are given in Table 2. A great majority of RRs occurred during the first 6 months after starting MDT whereas, the episodes of ENL occurred at a higher frequency in the second or third year after starting MDT.

Late reactions. Late reversal reactions were seen in 4.2% (47/1106) of PB patients and 5.3% (79/1494 patients) with MB disease. The majority of late reactions in the multibacillary group were observed in patients with borderline lepromatous (BL) disease. The incidence of late RR was highest during the first 2 yrs after being released from treatment (RFT). Even though the decline in the incidence of RR began early after the initiation of therapy, and most reactions occurred during the first 2 yrs, a few continued to occur until 7 yrs after RFT.

Late ENL reactions were seen in only 3% (45/1494) of MB [BL and polar lepromatous (LL)] patients. Late ENL, though mild and usually not associated with significant constitutional symptoms, continued to occur for up to 8 yrs after completion of MDT. Of these patients, 15 were treated be-

TABLE 2. *Time of onset of reactional episodes.*

Period	Pauibacillary				Multibacillary (N = 1494)			
	BT (N = 1106)		BB (N = 82)		BL (N = 902)		LL (N = 510)	
	No.	%	No.	%	No.	%	No.	%
Reversal reactions								
At registration	228	44.5	18	27.3	379	49.0	2	40
0–6 months	144	28.1	20	30.3	191	24.7	3	60
7–12 months	65	12.6	15	22.7	114	14.7	—	—
2nd year	46	9.0	13	19.7	46	5.9	—	—
≥3 years	29	5.7	0	0	43	5.5	—	—
Total	512	100	66	100	773	100	5	100
ENL Reactions								
At registration	—	—	—	—	35	19.4	142	20.1
0–6 months	—	—	—	—	19	10.5	91	12.9
7–12 months	—	—	—	31	17.2	123	17.4	
2nd year	—	—	—	—	59	32.8	192	27.2
≥3 years	—	—	—	—	36	20.0	157	21.8
Total					180	100%	705	100%

TABLE 3. *Risk factors for developing reversal reactions (RR).*

Risk factors	Patient group PB/MB/Both	No.	Rate ratio* (95%CI)	p value
Spectrum	PB	314/1106	0.69 (0.58–0.81)	p <0.01
	MB	544/1494		
Age (years)				
≤20	Both	120/357	1.0 (0.81–1.3)	p >0.1
>20	Both	738/2243		
Sex				
Male	Both	510/1634	0.80 (0.68–0.95)	p <0.05
Female	Both	348/966		
Extent of clinical disease				
≥6 skin lesions	Both	544/858	2.5 (2.1–2.9)	p <0.01
≥2 nerves involved	Both	523/858	2.4 (2.0–2.8)	p <0.01
≥3 Body areas involved	Both	544/858	2.8 (2.2–3.1)	p <0.01

*Rate ratio adjusted for the influence of age and sex

fore 1994 and the remaining 30 with fixed duration regimen (24 months) (p <0.01). However, there was no statistically significant difference among the number of MB patients manifesting late RRs treated before 1994 (43/79) and those treated with fixed duration regimen (36/79) (p >0.1).

Recurrent reactions. Of the 858 patients who manifested reversal reactions, 252 (29.4%) had ≥2 episodes and the remaining 606 (70.6%) had only a single episode of RR. Cumulative incidence of recurrent reversal reaction was 9.7% (252/2600) among all of the patients. The presence of a reversal reaction at the time of initial presentation or during the first year of treatment was more frequently associated with an increased risk of having another episode occurring later on.

Out of the total patients who experienced ENL, 217/337 (64.4%) experienced more than one episode. The median number of episodes was 4 and the time between the first and last episode averaged 34 months (range 5 to 96 months). A considerable number of patients (51/217, 23.5%) had more than ≥4 episodes of ENL over a period of observation varying from 3 years to 8 years, with no other identified risk factor except a higher BI (BI ≥3).

Risk factors. Female gender, multibacillary disease, and widespread disease (≥3 body areas involved, ≥6 skin lesions, or ≥2 peripheral nerve trunks involvement) were statistically significant risk factors for developing reversal reactions. The strongest association was observed between the extent of clinical disease and the risk of developing RR. Of the 858 patients manifesting RRs, 544 (63.4%) had ≥3 body areas involved and/or ≥6 skin lesions, and 523 (61%) had ≥2 nerve trunk involvement. Age was not found to be a significant risk factor for reversal reactions (Table 3).

Risk factors for developing ENL reactions are given in Table 4. Lepromatous leprosy, female gender and higher BI (≥3) were significant risk factors, whereas age was not.

DISCUSSION

Incidence. Much is known about the epidemiology of reactions, but their incidence in the period after MDT is less well documented because of lack of long term follow-up ([6]). Various estimates of the frequency of reversal reactions have been given by several authors ([1, 6, 17]). Published reports indicate that the frequency of RR at the time of diagnosis varies between 2.6% and 6.4% ([6]) though a much higher figure of 28% was reported in a hospital-based study from Nepal ([17]). In our study, this figure was 24.1%. Other studies have reported relatively lower total figures of 9.1% from Hyderabad, India ([9]) and 16.5% from Ethiopia ([14]), probably reflecting a variable proportion of PB/MB cases and the use of mixed case definitions used. Figures for the percentage of patients manifesting RRs at any time vary from

TABLE 4. *Risk factors for development of ENL reactions.*

Factors	Variables	No.	Rate ratio*	p value
Disease group	BL	95/902	.12 (0.09–0.17)	p <0.01
	LL	242/510		
Age	<20	34/238	1.1 (0.75–1.6)	p >0.1
	>20	303/2322		
Sex	Male	192/1634	.75 (0.59–0.95)	p <0.05
	Female	145/966		
BI	<3	120/2109	07 (0.05–0.09)	p <0.01
	≥3	217/491		

*Rate ratio adjusted for the influence of age, sex and bacteriological index

3.5% among PB cases in Malawi ([1]) to 47.5% among MB cases in Zaire ([6]). Due to the use of widely different case definitions, it is difficult to compare the frequencies of RR in PB and MB patient groups in studies published from different centers. Other factors contributing to such variation could be the time between diagnosis and beginning MDT, duration of MDT, duration of steroid regimen, and quality of the local leprosy control program. Overall 33% of all patients in our study developed RR at some time during treatment and follow-up, including those with a reaction at presentation.

ENL reactions were reported to occur in more than 50% of lepromatous leprosy (LL) cases and in about 25% of borderline lepromatous (BL) cases in the pre-MDT era ([7]). The incidence of ENL reactions appears to have fallen with the introduction of MDT, possibly due to the combined bactericidal effect of rifampicin and the anti-inflammatory effect of clofazimine in suppressing ENL ([8]). A hospital-based study from Nepal reported a high frequency of ENL reactions (28.6%) in LL, but only 7.5% in BL cases ([5]). In the present study, 47.4% of LL cases and 10.5% of BL cases manifested ENL reactions. The lower incidence of ENL among patients treated before 1994 could be because of the persisting anti-inflammatory effect of clofazimine till bacterial clearance was achieved. Field studies have reported a rather lower incidence of ENL such as 12% in LL and 3.6% in BL from Ethiopia ([9]), and 2.1% of all MB patients from Bangladesh ([10]). The varied frequency of ENL in reported studies could be due to patients in the field screened for reactions vs. patients reporting to the hospitals for reactions. Most of our patients were self-reporting having reactions severe enough to force them to seek treatment from a hospital rather than field-based clinics. This could be one reason for relatively higher figures for ENL in our center.

In reactions (RR or ENL) involvement of the skin and nerves occurred either singly or together. Of the total number of reactions at the time of presentation, 31.7% had only cutaneous involvement, whereas 68.3% had involvement of both skin and nerves. In a retrospective analysis of reversal reactions in a study from Hyderabad, India, 43.1% had only skin lesions, 31.8% had only neuritis, and 22.7% had both skin lesions and neuritis ([6]). Such observations emphasize that neuritis can occur along with inflammatory skin lesions or independently. Therefore, even very mild symptoms suggestive of neuritis should be taken seriously and nerves should be palpated on each visit to detect early signs of nerve inflammation, regardless of presence or absence of reaction involving skin.

Time of onset of reactions. Significantly, 30.9% of our patients presented to us because of reactions, in spite of having symptoms suggestive of leprosy for months or years. In a hospital-based study from Hyderabad, India, Lockwood, *et al.* ([6]) noted reactions in a strikingly high percentage of their patients (41.3%) at the time of presentation. It is obvious that many patients seek treatment only when they get frightened by the sudden development of such lesions particularly over face, or painful symptoms of neuritis due to reaction.

Although it is known that the reversal reactions occur most frequently within 6 to 12

months after starting treatment ([4, 11]), most previous studies did not report long term follow-up. In the AMFES data (Ethiopia), RR were reported to occur as late as 5 yrs after the start of treatment in both PB and MB patients ([12]). Our study also supports the fact that though the incidence of RR was found to decline gradually, reactions continued to occur for 7 years, though in very few patients. However, in India the longest interval reported between treatment and reaction is 6.5 years ([6]).

The majority of ENL reactions after starting MDT occurred in the second or third year and the recurrence of attacks was mostly noted in the same period, though the reactions continued to occur up to 8 yrs after RFT.

Late reactions. The percentage of patients developing late RR in both PB and MB groups was 4.2% and 5.3%, respectively. In a study from Thailand, 2.7% of PB patients and 9% of MB patients developed a late reversal reaction ([15]). In Malawi, 3.5% of PB patients developed late reactions during the first 4 yrs of follow-up ([2]). In a cohort of MB patients (treated with MDT for 2 yrs or longer until split-skin smear tested negative) from Karigiri, India, only 1.1% experienced reversal reactions during almost 10 yrs of surveillance ([18]). Late RR is known to occur mostly within the first 3 to 4 yrs after RFT ([1, 15]) as was also observed by us. In the absence of a clear definition for late RR and different MDT regimens used in various studies, an exact comparison of the frequency of late RRs is not possible.

Late ENL reactions were recorded in 3% of our MB cases. The majority of these episodes consisted of a few ENL lesions, which were mostly associated with only mild cutaneous and constitutional symptoms.

Recurrent reactions. Recurrent episodes of reversal reactions are an important clinical phenomenon, which may result in continuing nerve damage and add on to the degree and number of impairments. In our study, 9.7% patients developed recurrent episodes of reversal reaction. Almost half of these episodes occurred within 3 months of stopping the course of prednisolone that had been administered for the previous reaction. Strikingly, in a hospital-based study from Hyderabad, India, 33% of patients with RRs had recurrent episodes ([9]). The immune suppression in some of these patients may have been for of too short a duration, or hospitals may be more likely to get the severely affected problem patients, which require still longer treatment with steroids or some other adjuvant therapy. Possibly, Naafs, *et al*. may be right when they suggest that immunosuppressive treatment should continue throughout the period when the antigen load is sufficient to trigger the cell mediated immune response ([10, 11]).

Of all patients who manifested ENL, 64.3% had recurrent episodes. In the AMFES cohort (Ethopia), 63% of all cases with ENL had more than one episode, and 31% of all ENL cases manifested 5 or more episodes over a period of more than 2 yrs. In general, recurrence in episodes of reactions is more common in ENL than in RR, and approximately one-third of patients with ENL reactions go on to have recurrent episodes ([14, 16]). Patients must be warned of this possibility and be educated to return for follow-up, and clinicians should also be aware to diagnose even very late reactions in post-elimination era. Though it could be in variance to other proposed definitions (Transactions of 16th International Leprosy Congress), we suggest that a patient could be labeled as having "chronic ENL" if he needs continued antireaction treatment for a period of 6 months or more.

Risk factors. Risk factors for RR identified to be significant in this study were female gender, and disseminated disease (extent of clinical disease measured by involvement of a number of body areas, nerves, and skin lesions) at the time of diagnosis. PB patients had less risk of developing reversal reactions than MB patients. Patients with three or more body areas involved or having ≥6 skin lesions had about twice the risk of developing RR than those with limited disease (63.4% vs. 36.6%). Similar observations (>10 skin lesions) have been made by Van Brakel, *et al*. ([17]), which suggested that this can be of considerable importance for control programs, to identify patients at risk of developing reactions. They argued that "body area" may just be a proxy indicator for the bacteriological index or multibacillary end of the leprosy spectrum. Like our observation,

they also noted similar association within the borderline tuberculoid (BT) patient subgroup, indicating that body area count is useful indicator of the risk of developing RR. Pregnancy and lactation are reported to be risk factors for RR and ENL ([6, 8]), but the association has not been quantified and remains unclear. Leprosy lesions over the face have also been observed to develop RR more frequently ([3]). However, the relation between pregnancy or lactation and leprosy reactions, the significance of a patch over the face as a risk factor for developing reversal reactions, could not be statistically analyzed in the present study due to lack of complete information in the records.

For ENL, the risk factors identified in our study were lepromatous leprosy, female gender, and higher bacteriological index (≥3). For recurrent ENL, a number of risk factors like age, sex, spectrum of disease were analyzed, but only high BI (≥3) was found to be statistically significant. In AMFES cohort (Ethopia), no specific risk factor for recurrent ENL could be identified except age, between 20 and 45 yrs ([14]). In our study, though the majority of cases were in this age range, correlation with any age group could not be confirmed. ENL reactions are reported to occur throughout pregnancy and lactation, and may be severe and recurrent; however, because of incomplete information as stated above, this relationship could not be anlyzed in our cohort.

In conclusion, this is the largest series of patients with long term follow-up, delineating the epidemiology of reactions in leprosy from India. RR and ENL are common complications in leprosy patients in India. Female gender, multibacillary leprosy, and extensive disease were found to be major risk factors for occurrence of RRs. The majority of RRs occurred within 12 months of starting MDT, and then the incidence declined gradually but the reactions continued to occur until 7 yrs after RFT. For ENL, lepromatous leprosy, female gender and higher bacteriological index (≥3). Significant risk factors were approximately one-third of patients with ENL reactions go on to manifest recurrent episodes spread out over a period of more than 2 yrs requiring specialized expertise to manage them. Though leprosy is expected to be eliminated from all nations by 2005, even those patients who have successfully completed their treatment will continue to manifest with late or recurrent reactions in settings of poorly available expertise or services to manage these episodes.

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