

## Lepra reactions: A study of 130 cases from Pakistan

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### Abstract

**Objective:** To determine the occurrence and characteristics of lepra reactions in leprosy patients.

**Methods:** The retrospective study was conducted at the Marie Adelaide Leprosy Centre, Karachi, and comprised data of patients admitted between January 1, 2013, and December 31, 2015, for the management of lepra reactions. Data was noted on a detailed proforma and was analysed using Microsoft Excel and applying chi-square test.

**Results:** Of the 130 cases, 95(73%) were males and 35(27%) were females. Mean age at onset of the first episode was 39±14 years. Borderline lepromatous was the most common classification 76(58%), with 40(53%) of them having type 1 reaction as the first episode and 36(47%) having a type 2 reaction. Risk factors associated with recurrence were skin lesions, fever, lymphadenopathy and type of reaction ( $p<0.05$ ).

**Conclusion:** Healthcare providers need to be aware of the clinical manifestations of lepra reactions in order to diagnose them early.

**Keywords:** Leprosy, Lepra reactions, Type 1 reversal reactions, Erythema nodosum leprosum, ENL, Peripheral neuropathy, Neuritis. (JPMA 71: 2317; 2021) DOI: <https://doi.org/10.47391/JPMA.07-849>

### Introduction

Leprosy is a chronic granulomatous disease caused by an acid-fast bacillus, *Mycobacterium (M.) leprae*, which does not grow in vitro. It mainly affects the skin and peripheral nerves.<sup>1</sup>

The Ridley-Jopling classification divides the disease into five groups based on the cell-mediated immunity (CMI) of the host. In the tuberculoid type (TT), CMI is high. The three borderline types, borderline tuberculoid (BT), mid-borderline (BB) and borderline lepromatous (BL), are immunologically unstable, while the lepromatous (LL) type has low CMI.<sup>2</sup>

Lepra reactions are immunological complications of leprosy and are mainly of two types. Type 1 (reversal) are delayed hypersensitivity reactions and occur in the three borderline types of the disease. Type 2 erythema nodosum leprosum (ENL) reaction is an immune complex disorder and occurs in BL and LL types.<sup>3</sup>

Type 1 reactions are characterised by acute inflammation of skin lesions and acute neuritis, causing nerve damage, with anaesthesia and muscle weakness. Type 2 ENL reaction is a systemic disorder accompanied by fever, crops of painful red nodules, myositis, arthritis, lymphadenitis and neuritis. Uveitis and orchitis are the other complications.<sup>4</sup> Lepra reactions can occur before, during or after the completion of anti-leprosy multi-drug therapy

(MDT).<sup>5</sup>

According to the World Health Organisation (WHO) global leprosy update, 2018, the incidence and prevalence of leprosy in Pakistan was 0.2 per 100,000 population and 0.02 per 10,000 population, respectively.<sup>6</sup> A total of 342 new leprosy cases were detected in the country in 2018. Out of these, 245 (72%) were multi-bacillary (MB).<sup>6</sup> MB patients are said to be at a higher risk of developing reactions during the course of their disease.<sup>7</sup>

The current study was planned to determine the occurrence and characteristics of lepra reactions in leprosy patients.

### Materials and Methods

The retrospective study was conducted at the Marie Adelaide Leprosy Centre (MALC), Karachi, and comprised data of patients admitted between January 1, 2013, and December 31, 2015, for the management of lepra reactions. MALC is a 67-bed hospital where patients from all over the country and neighbouring Afghanistan are admitted for the management of leprosy and its complications. It has established and authentic record-keeping and follow-up procedures. After approval from the ethics review board of Aga Khan University Hospital (ALUH), Karachi, the sample was raised from among patients with a clear diagnosis of a lepra reaction at admission irrespective of the treatment status. All cases admitted for the management of a condition other than a lepra reaction were excluded.

The medical record of each patient was reviewed and data was collected using a proforma designed by MALC and AKUH teams.

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The proforma contained 44 variables in 4 sections, for demographic characteristics, clinical presentation, laboratory findings and treatment details. The section on clinical presentation covered information on the initial classification of leprosy, type of reaction on first admission, onset before, during or after chemotherapy, presenting complaints, skin lesions, enlarged nerves, sensory and motor dysfunction. A separate column was included for recurrence.

Data was analysed using Microsoft Excel, followed by descriptive and inferential analysis. Chi-square test was used to determine the significant difference between the expected and observed results.

**Results**

Of the 130 cases, 95(73%) were males and 35(27%) were females. Mean age at onset of the first episode of a lepra reaction was 39±14 years (range: 12-81 years). There were 88(68%) cases aged 25-54 years. There were 13(10%) cases classified as BT and all of them had type 1 reaction. There were 22(17%) BB case and all of them had type 1 reaction. Of the 76(58%) BL cases, 40(53%) had type 1 and 36(47%) had type 2 ENL reaction. All the 19(15%) LL cases had type 2 reaction. Overall, 75(58%) cases had type 1 and 55(42%) had type 2 reaction (Table 1).

In terms of onset, 57(44%) cases had a reaction at the time of diagnosis and before starting chemotherapy for leprosy; 50 (38%) had it after having started chemotherapy; and 23(18%) had it after discharge from treatment (Table 2).

At the time of diagnosis, 30(53%) cases had type 1 and 27(47%) had type 2 reaction. During treatment, 35(70%) had type 1 and 15(30%) had type 2 episode. After discharge from treatment, 10(43%) had type 1 and 13(57%) had type 2 reaction.

Among the 50 cases that had their first episode after starting chemotherapy, 14(28%) had it within the first month; the shortest duration reported was within 3 days which was a type 1 BB patient. Of these 14 cases, 11(79%) had type 1 and 3(21%) had type 2 reaction. Also, 20(40%) cases had the first episode within 2-6 months of treatment, with 17(85%) type 1 and 3(15%) type 2. Further, 11(22%) cases reported an episode during the 7-12 month period; 6(55%) type 1 and 5(45%) type 2. In 5(10%) cases, it occurred after 12 months of treatment; 4(80%) type 2 and 1(20%) type 1 (Table 3).

Out of 23 cases presenting with a reaction after discharge from chemotherapy, 14(61%) had it within a year of stopping treatment, with 7(50%) each having type 1 and type 2 episodes. In 3(13%) cases the first episode occurred within 2-3 years after discharge, with 2(66.6%) having

**Table-1:** Distribution of cases according to Ridley-Jopling classification.

Classification	Type 1 reaction n = 75 (58%)	Type 2 reaction n = 55 (42%)	Total n = 130	p-value
BT	13		13 (10%)	<0.05
BB	22		22 (17%)	
BL	40	36	76 (58%)	
LL		19	19 (15%)	

BT: Borderline tuberculoid, BB: Borderline borderline, BL: Borderline lepromatous, LL: Lepromatous

**Table-2:** Distribution of cases before, during and after chemotherapy.

Onset of reaction	Type 1 reaction n = 75 (58%)	Type 2 reaction n = 55 (42%)	Total n = 130	p-value
Before chemotherapy	30 (53%)	27 (47%)	57 (44%)	<0.025
During chemotherapy	35 (70%)	15 (30%)	50 (38%)	
After chemotherapy	10 (43%)	13 (57%)	23 (18%)	

**Table-3:** Occurrence of the first reaction episode during chemotherapy.

Onset of reaction	Type 1 reaction n = 35 (70%)	Type 2 reaction n = 15 (30%)	Total n=50 (38%)	p-value
1 month	11 (79%)	3 (21%)	14 (28%)	<0.025
2-6 months	17 (85%)	3 (15%)	20 (40%)	
7-12 months	6 (55%)	5 (45%)	11 (22%)	
After 12 months	1 (20%)	4 (80%)	5 (10%)	

type 1 reaction.

After 10 years of treatment cessation, 6(26%) cases presented with relapse; 1(10%) BT patient had a type 1 episode, while 2(20%) BL and 3(30%) LL cases had recurrent episodes of type 2.

In terms of recurrence, 60(46%) cases had a single episode; 37(62%) type 1 and 23(38%) type 2. Also, 54(42%) cases had 2-3 episodes; 10(19%) had both types of reactions; 27(50%) type 1; and 17(31%) type 2. Further, 16(12%) cases presented with four or more episodes, with 1(6.25%) BL case reporting a total of seven episodes; 3(43%) type 1 and 4(57%) type 2 within 18 months. Also, 1(6.25%) male patient aged 63 years at diagnosis relapsed 14 years after discharge from treatment, and then had four episodes of type 2 within a three-year period.

Six risk factors were significantly associated with recurrence; skin lesions (p=0.02), fever (p=0.02), lymphadenopathy (p=0.02), orchitis (p=0.04), leukocytosis (p=0.01) and the type of reaction (p=0.04).

Overall, fever was reported by 90(69%) cases; 39(43%) type 1 and 51(57%) type 2 reactions. Pain in limbs related to neuritis was reported by 89(68%) patients; 51(57%) type 1 and 38(43%) type 2 episodes. Joint pain was reported by 44(34%); 24(54.5%) type 1 and 20(45.5) type 2 presentation.

Inflamed plaques were seen in 61(47%); all (100%) type 1. Crops of painful erythematous nodules were found in

44(34%) cases; all (100%) type 2. Besides, 12(9%) others had ulcerating nodules, which was also a presentation of an ENL reaction. In 13(10%) cases of type 1 reaction, no evidence of a reaction was found in skin lesions and the main features were of neuritis.

Ulnar nerve enlargement was seen in 104(80%) cases, followed by radial cutaneous nerve 86(66%), and posterior tibial nerve 45(35%) cases.

Anaesthesia was seen in hands/feet of 76(58%) cases and hands/feet ulcers in 49(38%). Lagophthalmos due to facial nerve damage was detected in 17(13%) cases. Claw hand due to ulnar and median nerve damage was found in 30(23%). Foot drop due to common peroneal nerve involvement was reported in 4(3%) cases; all (100%) type 1.

Lymphadenopathy was found in 13(10%) cases; 10(77%) type 2 and 3(23%) type 1 who were classified as BL. Uveitis was diagnosed in 7(5%) cases; 5(71%) bilateral. Further, 6(86%) cases had uveitis during type 2 reaction, and in 1(14%) BL patient, it occurred during type 1. Orchitis was a feature in 23(24%) males; 17(74%) type 2 reaction and 6(26%) type 1. Among the latter, 4(66.6%) had episodes of both type 1 and type 2.

Slit-skin smear reports were available for 119(92%) cases. The bacteriological index (BI) score was 0 in 46(39%) cases, 1+ in 33(28%), 2+ in 18(15%), 3+ in 11(9%), 4+ in 5(4%), 5+ in 4(3.3%) and 6+ in 2(1.6%). Both cases (100%) with a 6+ score were classified as LL and had type 2 reaction. Of the 4 cases with 5+ score, 2(50%) each were BL and LL, and all 4(100%) had type 2 reaction.

## Discussion

The mean age of the patients in the present study is in line with earlier reports from Pakistan and Nepal.<sup>8,9</sup> Unlike the current study, Nepal, India and Bangladesh studies showed BT was more common than BL.<sup>9-11</sup> Also, BL cases had a higher prevalence of type 1 reaction compared to type 2.<sup>12</sup>

Type 1 reaction was more commonly seen at diagnosis and during treatment, while type 2 was more common after the discharge. Nepal and Bangladesh studies showed a higher percentage of reactions at diagnosis than during or after treatment.<sup>9,11</sup> In the Indian study, the incidence of type 1 reaction at diagnosis was higher than type 2, as was the case in the present study.<sup>10</sup> A study in the Philippines reported that 80% of the reactions after completion of MDT were type 1.<sup>13</sup>

Among those who had their first episode after starting chemotherapy, the majority had it within 2-6 months, and only 10% had it after 12 months. Majority of those having

a reaction after discharge had it within a year of stopping treatment. Other studies have also reported a higher proportion of type 1 reactions during the first 6 months of treatment, and type 2 later.<sup>10</sup> Reactions may remit and relapse over several years.<sup>14</sup> A study reported 43% relapse cases presenting with a reaction.<sup>15</sup>

The pattern of recurrence in the current study was similar to that reported from among Thai patients,<sup>16</sup> while the average number of reactions during treatment was 1.6 per patient in a Brazilian study.<sup>17</sup>

About 47% cases, all with type 1 reaction, presented with inflamed plaques on their skin. A study recorded erythematous, oedematous and scaly skin lesions in 96% cases of type 1 reaction.<sup>18</sup> Ulnar nerve was the most commonly found enlarged nerve in the current study. Facial, ulnar and common peroneal nerves are considered to be the most at risk in type 1 reactions.<sup>19</sup> Claw hands were found in 23% cases which was similar to an earlier study.<sup>20</sup>

Fever was found in 69% cases. A study reported systemic features, like fever and myalgia, in all type 2 cases.<sup>21</sup> Two different case reports of young, Pakistani males highlighted the occurrence of high-grade fever in type 2 reactions.<sup>22,23</sup>

The present study has limitations as it included primary data of leprosy patient with lepra reactions, and subjected it to secondary analysis. Patients with same reactions and hospital environment were difficult to find. Moreover, the data was never used before for the analysis.

## Conclusion

Lepra reactions occurred in leprosy patients before, during and after completion of treatment and some were recurrent. It is important for healthcare providers to know the varied clinical manifestations in order to be able to diagnose the reactions early enough.

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