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Original Article

# A clinicodemographic study of lepra reaction in patients attending dermatology department of a tertiary care hospital in Eastern India

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**Abstract**

***Objective*** To find the relative prevalence of lepra reactions among leprosy patients attending Dermatology out-patient department, the pattern of reactions in different types of leprosy and histopathological features of reaction.

***Methods*** The study was an institution-based, longitudinal study. A total 316 leprosy cases attended the Dermatology out-patient department (OPD) of a tertiary care hospital in Eastern India.

***Results*** Out of 316 leprosy patients, 58 (18.4%) were diagnosed to have lepra reactions and relative prevalence of type 1 and type 2 reaction was 10.4% and 7.9%, respectively. Among 58 patients, 50 fulfilled the inclusion criteria and were considered for final evaluation. Lepra reactions were common in patients over 30 years of age. There was a high male preponderance and the male to female ratio was 4.5:1. More than 60% of the patients belonged to the below poverty line. Farmers and laborers were more affected. Almost 62% of the patients were literates but most of them had primary education only. Type 1 reaction was more common in BT patients (50%), whereas type 2 reaction were more commonly seen in LL patients (32%). Erythema and swelling of the skin lesions, neuritis and edema of hands and feet were common features of type 1 reaction. Fresh crops of tender evanescent nodules, joint pain, neuritis and fever were common in type 2 reaction. Classical histopathological features were present in all the 50 slides examined. In type 1 reaction patients, lymphocytic infiltration (96%), dermal edema (93%), epithelioid cells (78%) and Langhans type giant cells (15%) were the common histological findings. Edema and foamy macrophages were seen in all cases of type 2 reaction patients. However, polymorphonuclear leucocytes and vasculitis were seen in 21 (95%) and 16 (73%) patients, respectively.

**Conclusion**
Lepra reactions, both type 1 and 2, occur in about 20% of leprosy patients. Early detection is warranted to avoid complications.

***Keywords***
Leprosy, lepra reaction

## Introduction

Leprosy is now a disease of underdeveloped countries of the world mainly concentrated in Asia, Africa and Latin America. Today the highest burden of patients are in India, Brazil, Myanmar, Madagascar, Nepal and Mozambique.[1,2] South-East Asia region accounts

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for 80% of global leprosy load, out of which India represents with 64% of cases.

Among the communicable diseases, leprosy is a leading cause of permanent physical disability. Due to the involvement of peripheral nerves, there is weakness of muscles and loss of sensations in hands, feet and eyes leading to ulceration and deformity. Social stigma and discrimination associated with leprosy are mainly due to disability and ulcers caused by the disease.

In the course of disease, leprosy is complicated by reaction. A reaction is appearance of symptoms and signs of acute inflammation in the leprosy patient. It represents episodes of acute hypersensitivity to *Mycobacterium leprae* antigens, due to disturbance in the pre-existing immunological balance.[3] Three types of reactions are recognized - lepra type 1 reaction (cell-mediated hypersensitivity), lepra type 2 reaction (immune complex-mediated) and Lucio phenomenon. Reaction in leprosy constitutes the main complication of the disease leading to serious consequences like nerve damage and deformities. Reaction may occur in any type of leprosy except the indeterminate type. Females, widespread disease, multibacillary disease, HIV, pregnancy, lactation and immunosuppression have been identified as risk factors.

Deformities in leprosy are mostly the consequence of reaction suffered during the course of the disease. Reactional states of leprosy are distinctive, tissue destructive, inflammatory processes that may occur before initiation of treatment, during treatment and sometimes, even after completion of treatment. It is important to recognize reaction promptly and treat them thoroughly, otherwise damage may be severe and irreversible, especially to nerve and eyes.

So far, few clinical studies have been done on lepra reactions with its correlation with clinical and histopathological features. In the present study we have analyzed the prevalence, clinicoepidemiological and histopathological features of the lepra reactions among leprosy patients attending OPD of a tertiary care center in Eastern zone of India.

## Methods

All previously treated cases, patients receiving treatment and new confirmed cases of leprosy with or without reaction were screened. Only those having features of lepra reaction were finally analyzed. Sample size was 50. Cases of leprosy and reactions in leprosy were diagnosed adopting the operational definitions as proposed by World Health Organization.

The study was an institution-based, descriptive study. Detailed history of patients, specially features of leprosy and reaction, were noted and recorded in case record form. Thorough clinical examination was done, and clinical photographs were taken after consent. Skin biopsy from the lesions was done in all cases and findings were recorded. Hematoxylin and eosin stain and Fite-Faraco stain were done.

## Results

During the study period, total 316 leprosy cases attended the Dermatology outpatient (OPD) of a tertiary care setup. Out of 316 leprosy patients, 58 (18.4%) patients were diagnosed with lepra reactions. Among 58 patients, eight patients did not give consent for biopsy and were excluded. Thus, 50 cases were considered for final evaluation. Relative prevalence of type 1 and type 2 reaction were 10.4% and 7.9%, respectively.

In our study population of 50 reaction patients, type 1 reaction was found to be more prevalent (developed in 28 patients, 56%) than type 2 (22 patients, 44%). Among the 28 patients who had type 1 reaction, 25 (50%) patients were borderline tuberculoid (BT), two (4%) were borderline lepromatous and one (2%) was suffering from pure neuritic leprosy. Borderline tuberculoid and pure neuritic patients suffered only from type 1 reaction. Among 22 patients who had type 2 reaction, 6 (12%) were of borderline lepromatous leprosy and 16 (32%) were of lepromatous leprosy. Lepromatous leprosy patients suffered only from type 2 reaction.

Out of 50 cases, males were 41 (82%) and females 9 (18%). Most of the female patients were in BT pole but difference was not statistically significant ($p$=0.2618, chi-square test). Among 41 male patients, 21 (42%) had type 1 reaction, and 20 (40%) had type 2 reaction. Among the 9 female patients, most of them (7 cases) suffered from type 1 reaction but this difference was not statistically significant ($p$=0.2789, $X^2$ test).

Majority of the patients (31 patients, 62%) belonged to the rural area whereas only 19 patients (38%) were from urban areas. The difference in residence among the study population was not found to be statistically different ($p$=0.9345, $X^2$ test). 19 (38%) cases were above poverty line and 31 (62%) cases were below poverty line. The difference in socio-economic condition among the study population was not found to be statistically different ($p$=0.6137, $X^2$ test). In our study population, most of the patients (62%) were literate and the remaining (38%) were illiterate ($p$=0.7842, $X^2$ test). Farmers (28%) constituted majority of lepra reaction patients. 18% of the cases were labourers, 16% were housewives, 14% were drivers, and 12% were business persons.

Recurrence was found only in 10 (20%) patients in our study population. Among 28 patients of type 1 reaction, 5 (10%) patients had multiple episodes during the study period. Similarly among 22 patients who had type 2 reactions, 5 (10%) patients had multiple episodes during the same period. Recurrence of reaction was not found to be statistically different between two types of reaction ($p$=0.9432, $X^2$ test).

In the present study, fever was the most common systemic symptom (21 patients, 42%) followed by joint pain (17 patients, 34%), eye involvement (10 patients, 20%) and testicular pain (6 patients, 12%). Fever was the only systemic feature in type 1 reaction, though it was statistically more prevalent in type 2 reaction ($p$ <0.0001, $X^2$ test).

In the present study, 34% patients showed reaction (mostly type 2) while on MDT. Physical exertion showed association in 12% patients (all of them had type 2 reaction) and in 54% no association could be found.

In the present study, lesions affected with reaction were distributed symmetrically in most (42%) of the patients. Among type 1 reaction most of them (18 in 28, 64%) were having bilateral asymmetrical cutaneous lesions. Type 1 reaction mostly presented with erythematous, scaly, edematous skin lesions in 27 (96%) cases **(Figure 1** and **2)**. Association of neuritis along with skin lesions occurred in 10 (36%) cases, while only 1 (3%) patient presented with neuritis alone (pure neuritic Hansen's). Edema of hands and feet were initial presenting symptom in 3 (11%) cases.

**Figure 1** Borderline tuberculoid (BT) leprosy with type 1 reaction on face.


**Figure 2** Borderline tuberculoid leprosy with severe type 1 reaction, mimicking psoriatic plaque.

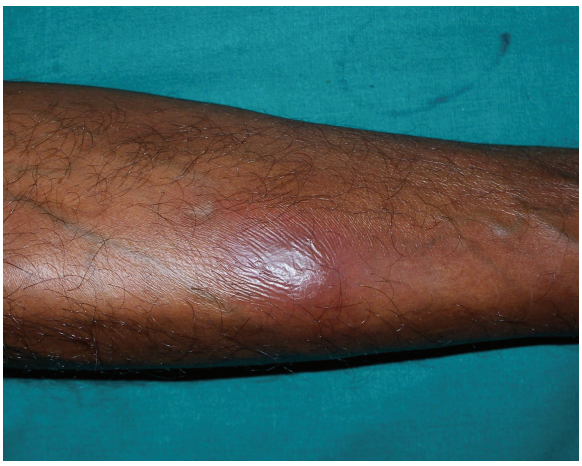

**Figure 3** Painful, erythematous nodule of erythema nodosum leprosum on leg.

**Figure 4** Erythema multiforme like lesions of erythema nodosum leprosum.

**Figure 5** Ear involvement in type 2 reaction.

In type 2 reaction, erythematous, tender, evanescent nodules were seen in all cases (**Figure 3-5**). Neuritis along with skin lesions was present in 18 (82%) cases; vesicles, bullae, ulceration and necrosis in 6 (27%) cases and edema of hands and feet in 9 (41%) cases.

In our study, type 1 reaction patients showed lymphocytic infiltration (96%), dermal edema (93%), epithelioid cells (78%) and giant cells (Langhans type) (15%) as the common histological findings. In type 2 reaction patients edema, foamy macrophages were seen in all cases. Polymorphonuclear leucocytes and vasculitis were seen in 21 (95%) and 16 (73%) patients, respectively.

**Discussion**

Reaction in leprosy is the main complication of the disease which can lead to serious consequence like nerve damage and deformities. Reaction is an important problem both for the patients and for the treating physician. The appearance of reactions not only indicates worsening of the disease but also raises doubts about curability of the disease.

In our study, 316 leprosy cases attended our OPD, out of which 58 patients (18.4%) were diagnosed as having lepra reaction and relative prevalence of type 1 and type 2 reaction were 56% and 44%, respectively among all the leprosy patients. In other studies, frequency of type 1 reaction at the time of diagnosis varies between 2.6% and 6.4%[4] though a much higher figure of 28% was reported in a hospital-based study form Nepal,[5] and 24.1% from Chandigarh.[6] The exact prevalence of type 2 reaction is not known. However, it is widely accepted that type 2 reaction is less common than type 1 reaction. Among the finally analyzable cases with lepra reaction, the relative prevalence of type 1 reaction was 56% (among 50) and type 2 reaction 44% (among 50).

Leprosy affects both the sexes. However, the incidence and prevalence of leprosy appears to be higher in males than in females in most regions of the world, with male to female ratio being 2:1. In our study too, we found a male preponderance of leprosy with 41 males and nine females. Among 41 male patients, 21 (42%) had type 1 reaction, and 20 cases (40%) had Type 2 reaction. Among the nine female patients, most of them suffered from Type 1 reaction (7 cases) but this difference was not statistically significant.

Ponnighas *et al*.[7] have observed highest incidence of leprosy amongst those persons who lived in poor conditions resulting in overcrowding and poor sanitation. Generally leprosy is a disease of the poor class and reactions are also common in this group which has a very low literacy level. In our study, reactions were more prevalent among poor and rural population, 19 (38%) cases belonged to the above poverty line and 31 (62%) cases to the below poverty line. Majority of the patients (31 patients, 62%) had rural background whereas only 19 patients (38%) were from urban areas. In our study population, most of the patients (62%) were literate but most of them had not received higher education.

Type 1 reaction is more common than type 2 reaction. Type 1 reaction is usually observed in borderline spectrum (BT, BB, BL) of the disease except with very rare reports in lepromatous leprosy (LL). Type 2 reaction (ENL) occurs mostly in lepromatous leprosy (LL) and sometimes in borderline lepromatous leprosy (BL). LL patients with high bacillary index are more prone to get ENL. Reactions may occur spontaneously or may be precipitated by intercurrent infections (viral, malaria etc.),

anemia, mental and/ physical stress, puberty, pregnancy, parturition or surgical interventions. Before the introduction of MDT, treatment with anti-leprosy drugs had been one of the precipitating causes of reactions. In our study, population of 50 reaction patients, type 1 reaction was found to be more prevalent (developed in 28 patients, 56%) than type 2 (22 patients, 44%).

Among the 28 patients who had type 1 reaction, 25 (50%) patients were of BT, two (4%) of BL and 1 (2%) suffered from pure neuritic leprosy. BT and pure neuritic patients suffered only from type 1 reaction. Among 22 patients who had type 2 reaction, 6 (12%) were of BL and 16 (32%) were of LL. LL patients in our study suffered only from type 2 reaction.

In the present study, 34% patients showed reaction (mostly type 2) while on MDT. Physical exertion showed association in 12% patients (all of them had type 2 reaction) and in 54% no association could be found.

It is mentioned in literature that the erythema and swelling of the existing lesions and neuritis are the predominant features in type 1 reaction along with mild constitutional features, like fever.[8,9] In the present study, we found similar lesions in type 1 reaction mostly presenting with erythematous, scaly, edematous skin lesions in 27 (96%) cases. Association of neuritis along with skin lesions was seen in 10 (36%) cases, while only 1 (3%) patient presented with neuritis alone (pure neuritic Hansen's disease). Edema of hands and feet was initial presenting symptom in 3 (11%) cases. Fever was the only systemic feature in type 1 reaction. In the study of Lockwood *et al*.[10], 43.1% had skin lesions alone, 22.7% had both skin lesions and neuritis and 31.8% had only neuritis.

ENL lesions are most characteristic lesions of type 2 reaction, which occur as crops of abruptly appearing, oval or round, erythematous, warm, evanescent, tender nodules, blanching on pressure, varying in size from 0.5-3cm, appearing in apparently normal skin and / or subcutaneous tissue. It usually occurs bilaterally and symmetrically, lasting from 2-3 days to few weeks without peripheral extension of the lesions. Pustulation is rare, although vesiculation and ulceration may occur in severe reaction. ENL lesions can be papular, plaque, vesicular or bullous, erythema multiforme like, pustular or frankly necrotic.[11,12]

Any or all of the following symptoms and signs may be associated with ENL, or may occur without ENL, and all are manifestations of type 2 reaction: fever and malaise, nerve pain, periosteal pain, muscle pain, pain and swelling of joints, rhinitis, epistaxis, acute iritis, painful dactylitis, swollen and tender lymph nodes, acute epididymo-orchitis and proteinuria.

In the present study, we found similar lesions. Erythematous, tender, evanescent nodules were seen in all type 2 reaction. Neuritis along with skin lesions were present in 18 (82%) cases; vesicles, bullae, ulceration and necrosis in 6 (27%) cases and edema of hands and feet in 9 (41%) cases. Fever was the most common systemic (90%) symptom followed by joint pain (77%), eye involvement (45%) and testicular pain (27%).

It has been described in literature that intense edema in the acute phase, marked rise in lymphocytes, occasional neutrophils and giant cells and a reduction in edema at the time of subsidence of reaction is seen in upgrading type 1 reaction. Edema, reduction in lymphocytes and higher number of macrophages with occasional Langhans giant cells is seen in downgrading type 1 reaction. In case of type 2 reaction

infiltration by neutrophils and vasculitis are predominant features.[13] In our study, among type 1 reaction patients lymphocytic infiltrate (96%), dermal edema (93%), epithelioid cells (78%) and giant cells (Langhans type) (15%) were the common histological findings. Edema and foamy macrophages were seen in all cases of type 2 reaction patients. However, polymorphonuclear leucocytes and vasculitis were seen in 21 (95%) and 16 (73%) patients of type 2 reaction, respectively. Thus, the histopathological findings in reactional leprosy depend upon the type of reaction and again in type 1 reaction it depends whether it is upgrading or downgrading. Histopathological findings can also help us to say whether the reaction is upgrading or downgrading in situations, where facilities for doing lepromin test are not available and also when the patient presents with reaction at the first visit.

## Conclusion

Reactional states of leprosy are distinctive, tissue destructive, inflammatory processes that may occur before treatment is initiated or after it has been completed. It is important to recognize reactions promptly and treat them thoroughly, otherwise damage may be severe and irreversible, speciously to nerves and eyes.

Around one-fifth leprosy patients developed reaction in our study which is consistent with other studies conducted globally. Thus early detection, education regarding the disease is an important weapon in the fight against the disease and its complications.

Education of the patients regarding leprosy, especially the reactions, goes a long way in containing the social problems. As the reactions are more common after initiating therapy, patients should be well informed about the possibility of occurrence of reactions and that they should not defer treatment which may compound to the problem.

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