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A Study to Observe the Incidence of Lepra Reactions After Initiation of Anti-Leprosy Therapy

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ABSTRACT

Background and Objectives: The study aimed to investigate the occurrence lepra reactions. Additionally, the study sought to examine the correlation between lepra reactions and the spectrum of leprosy. **Methods**: The study utilized a retrospective analysis of cases presenting with lepra reactions. Data on the types of lepra reactions, age and gender distribution, and clinical manifestations were collected and analyzed. Relevant literature and previous studies were reviewed and compared to the findings of the present study. **Results**: The study found that the overall occurrence of lepra reactions was 10.71%, with Type 1 lepra reaction being more prevalent than Type 2 lepra reaction. The age-wise distribution revealed a higher occurrence of T1LR in the 31-40 year age group and T2LR in the 41-50 year age group. Furthermore, lepra reactions were more common in males than females. The clinical manifestations varied for each type of lepra reaction, with specific skin lesions and extracutaneous features being predominant. **Interpretation & Conclusions:** The study concludes that Type 1 lepra reaction was more common in males aged 31-40 years, associated with BT leprosy, and characterized by specific skin lesions and extracutaneous manifestations. In contrast, Type 2 lepra reaction was more prevalent in males aged 41-50 years, linked to LL leprosy, and exhibited distinct clinical features. The findings highlight the need for targeted interventions focusing on education, prevention, early detection, and treatment for leprosy and lepra reactions. Furthermore, the study emphasizes the importance of future multi-centric studies to gain a comprehensive understanding of lepra reactions and their complications.

Keywords*: leprosy, lepra reactions, reversal reactions, erythema nodosum leprosum.*

INTRODUCTION

Leprosy is a chronic infectious disease caused by Mycobacterium leprae (M. leprae) which is an acid-fast rod-shaped bacillus[1]. Lepra reactions are one of the major problems faced during the management of leprosy. These are episodes of acute hypersensitivity to the antigen of Mycobacterium leprae brought about by a disturbance in the pre-existing immunological balance in leprosy patients. These reactions occur due to the dynamic nature of the immune response to M.leprae that can occur before, during, or following the completion of anti-leprosy therapy or multi-drug therapy (MDT). These reactions are of two major types – Type 1 and Type 2 Lepra reactions (LR).[2,3] Jopling W.H. et al. (1959) classified lepra reactions into 3 types:

- · Type 1 lepra reaction (T1LR) OR Reversal reaction
- · Type 2 lepra reaction (T2LR) OR Erythema Nodusum Leprosum (ENL)
- · Type 3 lepra reaction (T3LR) OR Lucio phenomenon[4]

Type 1 lepra reaction (T1LR) which is also known as "reversal reaction" is a Type IV hypersensitivity reaction that can occur in patients with borderline leprosy with cellular immune responses to M.leprae antigenic determinants. It is characterized by acute inflammation of pre-existing skin lesions or by the appearance of new lesions or neuritis. About,

95% of T1LR cases are diagnosed simultaneously with leprosy or during the first 2 years of MDT. They are commonly seen in the borderline spectrum of leprosy because of their immunological instability [i.e., BT, BB, BL]. A borderline patient may upgrade to TT to form secondary tuberculoid [TTs] or it may downgrade to subpolar LLs.[4-7]

Erythema nodusum leprosum (ENL) or type 2 lepra reactions (T2LR) are serious, difficult to manage, immune-complex mediated complications of lepromatous leprosy (LL) and borderline lepromatous (BL) leprosy. T2LR presents with skin lesions (red, painful, and tender subcutaneous lesions), fever, and systemic inflammation that may affect the nerves, eyes, joints, testes, and lymph nodes. Most of the T2LRs occur during the first year of MDT.[8]

Lucio phenomenon or Type 3 lepra reaction is one such rare reactional state seen peculiarly in the pure and primitive diffuse form of lepromatous leprosy and less commonly in borderline forms. This phenomenon was first described by Lucio and Alvarado in Mexico in 1852.[9-11]

Lepra reactions are responsible for most permanent nerve damage, deformity, and disability. Irreversible, progressive damage to peripheral nerves and tissue damage secondary to motor and sensory impairments are the most important consequences of leprosy. These result in physical impairments and the limitation of physical activities and social participation that are associated with leprosy.[12]

The classification of lepra reactions into three types (Type 1, Type 2, and Type 3) helps healthcare professionals understand the different immunological processes and clinical features associated with each type of lepra reaction in individuals affected by leprosy. This classification aids in guiding appropriate treatment strategies and management approaches for leprosy patients experiencing lepra reactions. Therefore, understanding the different types and manifestations of lepra reactions is crucial for effectively managing the complications associated with leprosy and minimizing permanent nerve damage.

The aim of this research study is to understand the epidemiology of different clinical manifestations of leprosy and lepra reactions. This research study aims to investigate the frequency and characteristics of different types of lepra reactions and their clinical manifestations in individuals affected by leprosy.

MATERIALS AND METHODS:

This retrospective study was carried out as an Indian Council of Medical Research Short Term Studentship 2022 (ICMR-STS) project on patients attending Department of Dermatology of a tertiary care centre and admitted to District Leprosy centre of Dahod district of Gujarat Ethical statement: Prior ethical clearance was obtained by the Institutional Ethics Committee to conduct the research. Participants were informed and written consent was obtained from each participant before the actual commencement of the study.

Study Design: A cross-sectional study design was employed to collect data of patients.

Study Participants: 168 patients suffering from leprosy were included in the study

Study Period: Information regarding present study was taken from data available at District Leprosy Centre of patients attending Department of Dermatology between April to September 2022.

Data Collection: Data regarding the demographic details, clinical features, treatment, and complications were reviewed and recorded on a case record sheet. The patients with incomplete medical records were excluded from the study.

Diagnostic Criteria and Classification: We used the classification of Ridley- Jopling to categorize the patients into the following- polar tuberculoid (TT), borderline tuberculoid (BT), mid borderline (BB), borderline lepromatous (BL), polar lepromatous (LL) types. We have also used the WHO classification of leprosy to categorize them as PB (Paucibacillary) and MB (Multibacillary). Type 1 reaction was diagnosed by erythema and edema of existing skin lesions or the appearance of new similar lesions with or without nerve tenderness or sudden impairment of sensory or motor function. Type 2 reaction was diagnosed by the appearance of crops of erythematous tender nodules with any one of the following, fever, arthritis, neuritis, edema of hands and feet, dactylitis, iritis, epistaxis, epididymo-orchitis, lymphadenitis. Neuritis was diagnosed by neural pain, nerve thickening, and nerve tenderness. Both Type 1 and Type 2 reactions were graded according to their severity.

Data Analysis: Data entry was done in Microsoft Excel and further statistical analyses were carried out using SPSS version 29.0. Descriptive statistics were used to study the prevalence different clinical features and types of lepra reactions. The data were presented in tabular and graphical format.

RESULTS:

In the present study, 168 leprosy patients were included of which 79 were females and 89 were males. The mean age of the study participants was 34 years.

Table 1: Distribution of study participants based on the clinical spectrum of leprosy

Clinical types	Number	Percentage
TT	12	7.14%
BT	49	29.17%
BB	14	8.33%
BL	30	17.86%
LL	34	20.24%
Indeterminate	8	4.76%
Pure Neuritic	16	9.52%
Histoid	5	2.98%

Based on the WHO classification, the proportions of PB and MB were 43.45% (n = 73) and 56.55% (n = 95) respectively. The overall occurrence of lepra reactions in total was 10.71% (n = 18) whereas the occurrence of T1LR and T2LR was 5.95% (n = 10) and 4.76% (n = 8) respectively (Table 1).

Table 2: Number of cases of lepra reactions in specific type of leprosy (RJ classification)

Type of Leprosy	Type 1	Type 2
TT	1	-
BT	6	-
BB	3	-
BL	-	3
LL	-	4
Histoid	-	1

The mean ages of T1LR and T2LR cases were 36 years and 43 years respectively. The occurrence of Type 1 LR was more common in the 31–40-year age group while the occurrence of Type 2 LR was more common in the 41–50-year age group. There were a total of 10 males and 8 females who presented with lepra reactions. Occurrences of lepra reactions in males and females were 61.11% and 39.89% respectively. The sex ratio for Type 1 LR and Type 2 LR were 3:2 and 5:3 respectively in this study.

The occurrence of skin lesions and hypoesthesia/anaesthesia were more prevalent while swelling of the leg and tingling/numbness were less prevalent. The most prevalent clinical feature was skin lesions while the least prevalent clinical feature was swelling of the leg.

BT was the most prevalent clinical type while Histoid was the least prevalent clinical type based on the spectrum of leprosy. Type 1 LR was most commonly found in BT leprosy patients while Type 2 LR was more commonly found in LL patients.

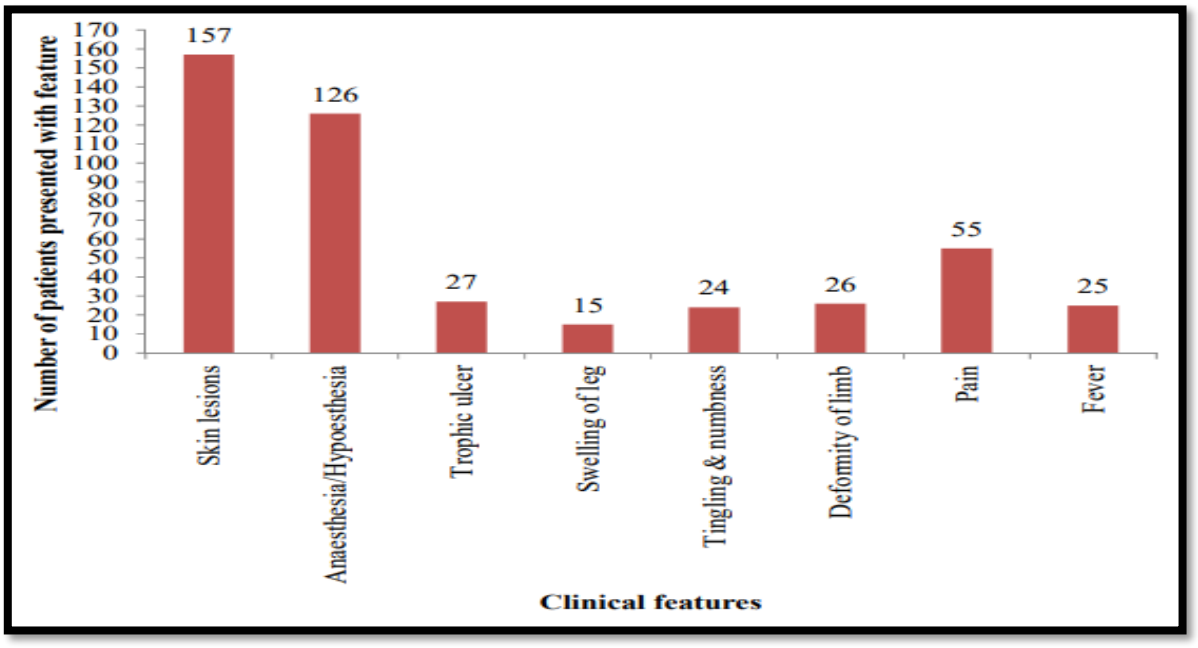

Figure 1: Epidemiology of different clinical features of leprosy in the study participants

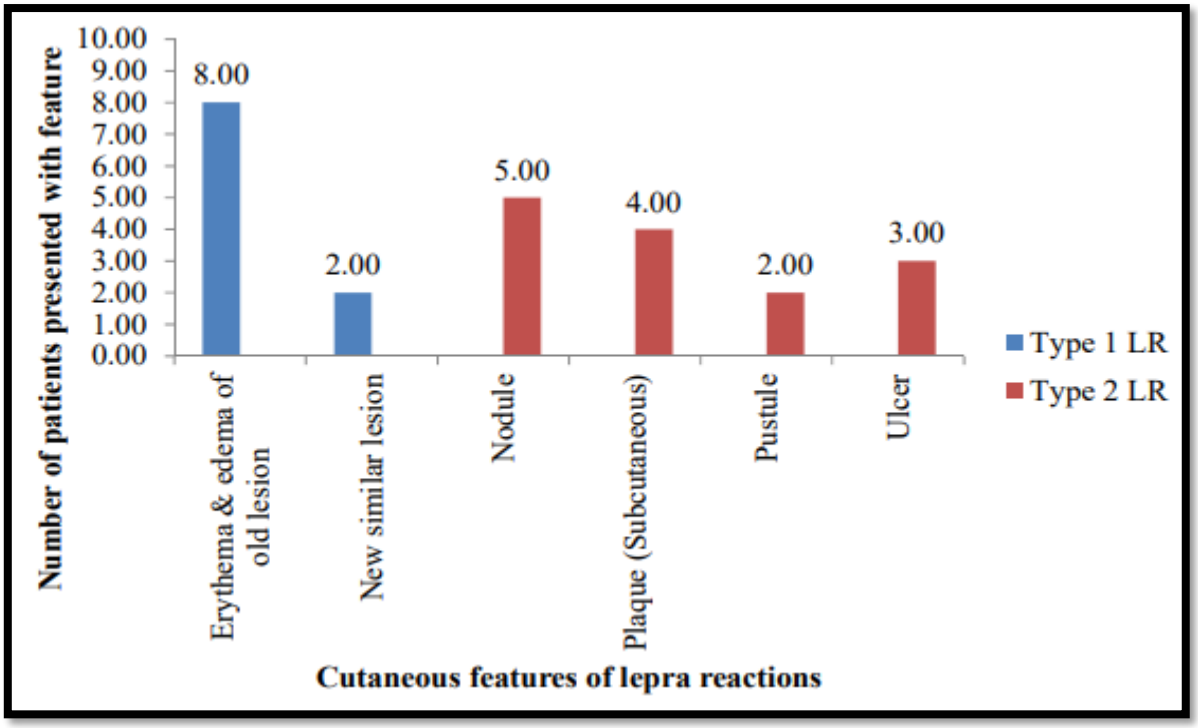

Figure 2: Epidemiology of Cutaneous features of lepra reactions

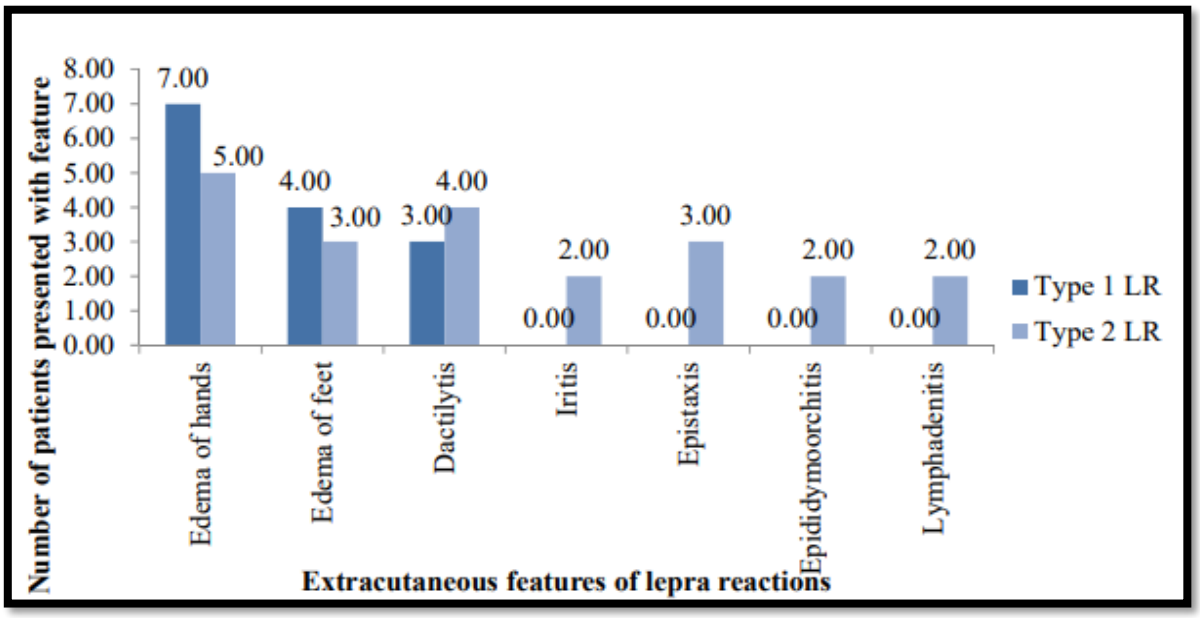

Figure 3: Epidemiology of extracutaneous features of lepra reactions

DISCUSSION:

A. Occurrence of lepra reactions and their types:

The overall occurrence of lepra reactions was 10.71% whereas the occurrence of T1LR and T2LR was 5.95% and 4.76% respectively. The occurrence of T1LR is higher than T2LR in the study.

Similar studies by P. Suchonwanit et al, E. Thomas et al., P. Nataraj et al., and S. Tabassum et al. show the occurrence of T1LR is higher than T2LR in the study which is in accordance of the present study.A study by S. Bezalel et al. shows results contrary to these findings. In his study, he found more occurrences of T2LR than T1LR.[13-17]

B. Age-wise occurrence of lepra reactions:

The present study shows that there were more occurrences of T1LR and T2LR in the 31-40 and 41- 50 years age group respectively. 1 case of T2LR was found in our study in the age group 20 years or below. So, the incidence

of T2LR was 87.5% in the above 20 years age group. A survey by Scollard et al. shows the highest incidence of T1LR in the 21–40-year age group and an 83% occurrence of T2LR in the above 20 years, age group. A survey by Bharathi et al. shows the incidence of T1LR was highest in the 21–30-year age group followed by the 31–40-year age group and did not find any case of T2LR in the 20 years or below age group.[2, 18]

C. Gender-wise occurrence of lepra reactions:

The present study shows lepra reaction is more common in males as compared to females. This can be correlated with studies of Suchonwanit, Nataraj, Scollard, et al., and Bharathi et al. [2, 13, 15, 18]

D. Occurrence of different spectrum of leprosy:

This study shows that T1LR was more common in BT (60%) while T2LR was more common in LL (50%). It was easily correlated with similar findings in the studies of Bharathi et al., and Sehgal et al.[18,19]

E. Clinical Features of Lepra Reactions:

In the case of T1LR, this study reported Skin lesions, anaesthesia/hypoesthesia, and pain due to neuritis as predominant clinical features. The most common skin lesions encountered were erythema and edema of old lesions while the most common extracutaneous manifestation was edema of the hand and feet. S. Bharathi mentioned in her study that the predominant clinical features of Type 1 reaction observed in our study were raised erythematous skin lesion [79.3%], neuritis [89.4%], and constitutional symptoms [36.8%].[18] Hastings mentioned that the erythema and swelling of the existing lesion and neuritis, are the predominant features in cases of Type I reaction along with mild constitutional features like fever.[3] Thus, these studies had shown similar findings about T1LR in accordance to the present study.

In the case of T2LR, this study reported crops of erythematous and tender nodules, subcutaneous plaques, ulcerative lesions, dactylitis, and edema of limbs as predominant features. Constitutional symptoms like Fever, arthralgia, and malaise were also common findings. Similar findings were reported in a study by S. Bharathi et al. except that in that study dactylitis was not so common.[18] Van Brakel et al. in the study conclude that presence of the following clinical signs is diagnostic of ENL i.e., multiple, tender nodules, with or without ulceration, neuritis (shooting or burning), fever, edema, involvement of other organs, e.g., Iritis, orchitis, and arthritis. The features are almost in concurrence with the present study.[5]

CONCLUSION:

The present study showed that most common type of lepra reaction among the participants was Type 1 lepra reaction. It was more common in males and 31-40 years of age. The most common clinical type associated with Type 1 lepra reaction was BT. The common skin lesions found in patients were erythema, and edema of old lesions while the most common extracutaneous manifestations were edema of the hand and feet. Type 2 Lepra Reaction was found to be more common in males and between 41-50 years of age. The most common clinical type associated with Type 2 lepra reaction was LL. The common skin lesions were crops of erythematous and tender nodules, subcutaneous plaques, and ulcerative lesions while common extracutaneous lesions were dactylitis and edema of limbs. Constitutional symptoms like fever, arthralgia, and malaise were also common.

This study provides valuable insights into the epidemiology of lepra reactions and its different clinical manifestations. The findings suggest a need for targeted interventions aimed at educating people about leprosy, lepra reactions and a need for preventive measures, early detection and treatment. Future multi-centric studies are warranted to learn about leprosy, lepra reactions and its complications.

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