Original Research Article

Leprosy reactions: a prospective study at tertiary care hospital of South Gujarat

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ABSTRACT

Background: Clinical diagnosis of early leprosy lesions is important as it is one of the leading causes of physical disabilities which cause social stigma leading to discrimination and isolation. Its diagnosis is based upon detailed cutaneous examination along with peripheral nerves. The objectives were to study associations between reaction types with type of leprosy and various deformities and disabilities relating to treatment for leprosy.

Methods: This is a hospital-based prospective, cross-sectional observational study. 110 clinically diagnosed Leprosy patients with reactions visiting Dermatology OPD were analysed after obtaining informed consent. Participants’ data were collected for demographic criteria, clinical history, past medical history and family history. Clinical examination of a study participant was performed. Collected data was entered in Microsoft excel worksheet and analysed for frequency distribution.

Results: All subjects were in a mean age of 38.03±14.37 years. 13.64% patients had positive family history of leprosy. 59 (53.64%) and 51 (46.36%) cases were of type 1 and type 2 reactions, respectively. Out of 59 patients with type 1 reaction, the most common presenting symptom was inflammation of pre-existing lesion observed in 35 (59.32%) cases while the most common presenting symptom of type 2 reactions was erythema nodosum leprosum seen in 34 (66.67%) cases. Type 1 reaction presented histopathologically as upgrading (67.80%) and downgrading reactions (5.08%). Histopathological finding in type 2 reaction were neutrophilic infiltration with macrophage granuloma seen in 54.90% cases.

Conclusion: It is important to identify reactions associated with leprosy and its treatment as they can significantly alter the morbidity of an affected individual.

Keywords: Leprosy, Reactions, Clinical, Parameters, Histopathology

INTRODUCTION

Leprosy is chronic infectious bacterial disease caused by Mycobacterium leprae. It affects skin, peripheral nerves, upper respiratory tract mucosa and eyes. 60% of global leprosy cases which comprise of approximately 1, 30,000 fresh cases from India are reported annually. The first authentic description of this disease has been reported from 600 B.C. The first direct evidence of leprosy with bone involvement was discovered in an Egyptian mummy of 2nd century B.C. Leprosy when untreated can result in disfigurement and disability, due to which it is feared and carries social stigma. Until introduction of Dapsone in 1940’s, no effective treatment for leprosy infected individuals was available due to which they were isolated and segregated from society.

Acute manifestations of Leprosy Reactions were reported by
pioneer leprologists, Danielssen & Boeck. They were first to identify reddish nodules associated with fever in nodular leprosy as a pointer of dissemination of disease.\textsuperscript{2} The term Erythema Nodosum Leprosum (ENL) was first employed by Murata oh Japan in 1912.\textsuperscript{3} Sir Leonard Rogers working in the Bengal cadre of Indian Medical Service used Ernest Muir’s clinical description of this disease during acute reactionary episode which comprised of sudden swelling, redness of existing lesions with appearance of new lesions associated with toxemia and fever.\textsuperscript{4} These reactions have been found to be occurring in three types of this disease are tuberculoid, lepromatous and borderline. International Leprosy Congress, Madrid (1953) had classified these associated reactions as Lepra reaction and Erythema Nodosum Leprosum (ENL). However, the panel on reactions at the VIII International Leprosy Congress at Rio de Janeiro (1963) did not agree with the this classification however, keeping in view its long and customary use, the term "lepra reactions" was retained and was included under three clinical conditions, they are Erythema Nodosum Leprosum (ENL); Erythema multiforme and Erythema necroticans. Reactions in tuberculosis leprosy pole were considered to be due to heightened immunological response to presence of M. leprae.\textsuperscript{4,5} Klokke et al confirmed this increase in immunity by isopathic phenomenon in response to various antigens. The Erythema Nodosum Leprosum reaction in lepromatous pole has been considered as an ‘Arthus phenomenon’. First evidence of the immune complex etiology of this reaction was provided by Wemambu et al.\textsuperscript{5}

Since past 35 years, prevalence of leprosy across the world has shown an increase from 8.4 cases per 10,000 populations in 1966 to 12 cases per 10,000 in 1985. There were 5.4 million registered cases of leprosy world-wide by the year 2000.\textsuperscript{6} In early 2000s, global prevalence of leprosy reduced significantly by 89% to less than 1 case per 10,000 population, thus, highlighting success of World Health Organization elimination program\textsuperscript{7}. Leprosy is a major communicable public health problem mainly within inter-tropical belt, with highest prevalence rates observed in Asia, Africa and South America.\textsuperscript{7} Approximately, three-quarters of world’s registered leprosy patients are residing in South-East Asian countries with India, Indonesia, Nepal and Myanmar accounting for 70% cases.\textsuperscript{8} Government of India initiated Leprosy Control Program in 1955 which was re-named as National Leprosy Eradication program (NLEP) in 1983. India achieved its elimination target of prevalence rate of less than one case per 10000 population in December, 2005.\textsuperscript{9} The current prevalence rate of leprosy in India is 0.68 per 10000 population.\textsuperscript{10} Though, incidence rate for June, 2011 was again found to be 10.28 cases per 10,0000. This indicated that leprosy is still an active disease and its transmissibility is still an issue.\textsuperscript{11} Leprosy more frequently occurs in closely spaced clusters of which family clusters are most important.\textsuperscript{12} Even with availability of multi-drug treatment (MDT), leprosy reactional episodes are adverse complications of leprosy. These episodes represent an exacerbation of host inflammatory processes which can manifest any time during disease process. Leprosy reactions may lead to deformities and associated disabilities which can evoke variable responses among individuals, their families and community which may be aversive behaviour, hatred, fear, stigma, social discrimination and ultimately, leading to socio-economic dehabilitation. Therefore, it is imperative to have knowledge regarding reactions’ types, various precipitating or risk factors, various clinical reactions and their courses, multi-drug therapy for preventive measures and early diagnosis of leprosy associated deformities and disabilities.

The aim of the study was to study various leprosy reactions while the objectives were to study association between reaction type with type of leprosy and various deformities and disabilities in relations to treatment for leprosy.

**METHODS**

This hospital-based prospective, cross-sectional study was conducted from a period of January 2014 to December 2014 after obtaining permission from scientific research committee and ethics committee of Government Medical College, Surat, Gujarat, India. This observational study was designed to analyze Leprosy reactions in 110 clinically diagnosed Leprosy patients with reactions visiting Dermatology Out-Patient Department. Informed consent was taken from all study participants after explaining them the study in local vernacular language. Inclusion criteria of the study were patients who signed the informed consent form and all the patients diagnosed with leprosy with any reaction that was currently on or had completed anti-leprotic treatment.

Exclusion criteria included participants who left the treatment or refused to continue with the study

Data collection carried out by collection of participants’ data for demographic criteria such as- age, sex, marital status, migration and clinical history which included symptoms at time of presentation, duration of anti-leprosy treatment, past medical history & family history.

Patient examination by clinical examination of a study participant was performed for evaluating the type of leprosy, peripheral nerve examination, sensory and motor examination, type of reaction and presence or absence of deformity.

All Participants were biopsied for histopathological examination. Participants were subjected to investigations like complete blood count, liver function test, renal function test, erythrocyte sedimentation rate, x-ray as per patient presentation and symptoms. After thorough analysis of all clinical details and pathological and/or
radiological examination, suitable treatment for reaction was provided.

Collected data was entered in Microsoft Excel Worksheet and analyzed for frequency distribution.

RESULTS

Age and sex distribution

The present study included 110 patients of leprosy reactions with a mean age of 38.03±14.37 years. Youngest patient was 10 years old while the oldest was 67 years. 5 (4.55%) patients were in age group of 5-14 years, 28 (25.45%) patients were in 15-30 years age group, 42 (38.18%) patients were in age range of 31-45 years, 26 (23.64%) patients were in 46 to 60 years, 9 (8.18%) patients were more than 60 years of age. 56 (50.90%) and 54 (49.09%) cases males and females, respectively, thus, the Male to female ratio was observed to be 1.03:1 (Table 1, Figure 1).

Types of leprosy

Borderline lepromatous leprosy was found to be the major type of disease comprising of 30% cases while 26.36% cases belonged to the Tuberculoid variety. 5.55% patients were suffering from mid-borderline group while 21.82% cases of lepromatous leprosy (Table 2).

Table 1: Age & sex distribution.

| Age (yrs) | Gender | Total (%) |
|-----------|--------|-----------|
|           | Male   | Female    |
| 5-14      | 3      | 2         | 5 (4.55)   |
| 15-30     | 15     | 13        | 28 (25.45) |
| 31-45     | 24     | 18        | 42 (38.18) |
| 46-60     | 11     | 15        | 26 (36.18) |
| >60       | 3      | 6         | 9 (8.18)   |
| Total     | 56     | 54        | 110 (100)  |

Table 2: Distribution of leprosy types.

| Type of leprosy | Total no. of cases | Percentage (%) |
|-----------------|--------------------|---------------|
| Tuberculoid     | 18                 | 16.36         |
| Borderline tuberculoid | 29     | 26.36         |
| Mid-borderline  | 6                  | 5.55          |
| Borderline lepromatous | 33     | 30            |
| Lepromatous     | 24                 | 21.82         |
| Total           | 110                | 100           |

Figure 2: Types of reactions in leprosy types.

Types of leprosy reactions and onset-time

In present study, out of 110 cases, 59 (53.64%) cases were of type 1 and 51 (46.36%) cases were of type 2 reactions. Of these, 8.47% cases (5/59) of type 1 reaction were newly diagnosed and were observed in 18 (16.36%), 29 (26.37%), 04 (3.64%), 08 (7.27%) and none (0%) of Tuberculoid, Borderline tuberculoid, mid-borderline, borderline lepromatous and lepromatous types of leprosy, respectively while type 2 reactions were observed in 02 (1.82%), 25 (22.73%), 24 (21.82%) and 51 (46.36%) cases of mid-borderline, borderline lepromatous and lepromatous types of leprosy, respectively and no type 2 reactions were reported in tuberculoid and borderline tuberculosis leprosy cases (Figure 3). In current study, type 1 reaction was observed in 15 (25.42%) cases within 3 months of initiating anti-leprosy treatment, whereas 20 (33.90%) cases reported type 1 reaction within 3 to 6 months and 12 (20.34%) cases reported within 6 to 9 months and 7 (11.86%) cases had type 1 reaction within 9 to 12 months. None of the patient presented with type 1 reaction after completion of ALT for duration of 12 months. 4 (7.84%) cases of type 2 reaction were observed on completion of ALT for 12 months (Figure 3).
neuritis, new cutaneous lesion, neuritis associated with deformity and edema of hands and feet which observed in 33.90%, 6.78%, 5.09% and 10.17% cases, respectively. Of 51 patients presenting with type 2 reaction, more than one symptoms were identified at the time of presentation.

In this study, the most common presenting symptom of type 2 reaction was ENL (erythema nodosum leprosum) seen in 34 (66.67%) cases. Other symptoms seen were neuritis, neuritis with deformity, bone pain and iritis which were observed in 15 (29.41%), 07 (13.73%), 20 (39.21%) and 9 (17.64%) cases, respectively (Table 4).

**Associated deformities with leprosy**

Presence of trophic ulcer was observed in a total of 20 (18.18%) cases, of which 9 cases were Borderline Lepromatous (BL), 9 cases (8.18%) were Lepromatous (LL) and 2 cases (1.82%) were Borderline Tuberculoid (BT). Claw hand was observed in 20 (18.18%) with highest number of 9 cases in BL (8.18%) followed by 6 cases of BT (5.45%), 3 cases of LL (1.5%), TT & BB (1 case each i.e., 0.5%). Digital resorption was noted in 09 (8.18%) cases with highest number of cases in BL (6, 5.45%) followed by LL (3, 1.5%). Saddle nose was observed in 7 (6.36%) cases wherein 5 cases (4%) belonged to LL and 2 cases (1.82%) were in Borderline Lepromatous leprosy. Wrist-drop was seen in 2 (1.82%) cases of Lepromatous leprosy while foot-drop was seen in 5 (4.55%) cases of which 2 cases (1.82%) had BT while 1 case (0.5%) each were of BB, BL & LL. Lagophthalamos was observed in 2 cases (1.82%) of which 1 each in BL and LL. Madarosis was observed in 6 (5.45%) cases of which 5 suffered from LL (4%) and one patient had BL (Table 5).

**Deformities associated with reaction and deformity rate**

Out of 59 patients presenting with type 1 reaction, trophic ulcer was present in 3.39% cases whereas claw hand and...
foot drop was seen in 11.86% cases and 3.39% cases respectively.

Also, out of 51 patients with type 2 reaction, trophic ulcer, claw hand, resorption of digits, saddle nose, wrist drop, foot drop, lagophthalmos and madarosis were present in 35.29%, 25.49%, 17.65%, 13.73%, 3.92%, 5.88%, 3.92% and 9.80% cases, respectively. In present study, deformity rate of type 1 reaction was 15.25% (9/59) and type 2 reaction was 49.02% (25/51) (Table 5).

**Sites associated with disabilities and reactions**

In present study, Feet were the most common site of disability followed by hands and eyes. Disability involvement of feet, hands and eyes were observed in 48.18%, 43.64% and 1.82% cases, respectively. In this study, out of 59 cases of type 1 reaction, 15 cases (25.42%) had disability of hands and 10 cases (16.95%) had disability of feet. None of the patient with type 1 reaction reported with ocular disability. Out of 51 cases of type 2 reaction, 33 cases (64.71%) had disability of hands, 43 cases (84.31%) had disability of feet and 2 cases (3.92%) had disability of eyes. Feet were found to be most common site of disability in type 2 reaction.

### Table 5: Deformities Associated with leprosy.

| Deformities Associated | TT | BT | BB | BL | LL | Total (% age) | Type 1 Reaction (n=59) | Type 2 Reaction (n=51) |
|------------------------|----|----|----|----|----|--------------|------------------------|------------------------|
| Trophic ulcer          | -  | 02 | -  | 09 | 09 | 20 (18.18)   | 2 (3.39)               | 18 (35.29)             |
| Claw hand              | 01 | 06 | 01 | 09 | 03 | 20 (18.18)   | 7 (11.86)              | 13 (25.49)             |
| Resorption of digits   | -  | -  | -  | 06 | 03 | 09 (8.18)    | 0                      | 9 (17.65)              |
| Saddle Nose            | -  | -  | -  | 02 | 05 | 7 (6.36)     | 0                      | 7 (13.73)              |
| Wrist drop             | -  | -  | -  | -  | 02 | 2 (1.82)     | 0                      | 2 (3.92)               |
| Foot drop              | -  | 02 | 01 | 01 | 01 | 5 (4.55)     | 2 (3.39)               | 3 (5.88)               |
| Lagophthalmos          | -  | -  | -  | 01 | 01 | 2 (1.82)     | 0                      | 2 (3.92)               |
| Madarosis              | -  | -  | -  | 01 | 05 | 06 (5.45)    | 0                      | 5 (9.80)               |
| Total                  | 01 | 10 | 02 | 29 | 29 | 71 (64.55)   |                        |                        |

### Table 6: Histopathological correlation of various leprosy types.

| Leprosy                  | Type 1 reaction | Type 2 reaction | Histopathology (%) | Confirmed | Inconclusive | Total |
|--------------------------|-----------------|-----------------|--------------------|-----------|--------------|-------|
| Tuberculoid (TT)         | 18              | -               | 14 (77.78)         | 04 (22.22) |              | 18    |
| Borderline Tuberculoid (BT) | 29             | -               | 22 (75.86)         | 07 (24.13) |              | 29    |
| Mid-borderline (BB)      | 04              | 02              | 04 (66.67)         | 02 (33.33) |              | 06    |
| Borderline lepromatous (BL) | 08             | 25              | 20 (60.61)         | 13 (39.40) |              | 33    |
| Lepromatous (LL)         | 00              | 24              | 13 (54.17)         | 11 (45.83) |              | 24    |
| Total                    | 59              | 51              | 73 (66.36)         | 37 (33.64) |              | 110   |

**DISCUSSION**

This study found a male-female ratio of 1.03:1 while Sharma et al in a similar study conducted in a tertiary care hospital located in Delhi found a male-female ratio of 2.79:1. This high male to female ratio was attributed to higher numbers of migrating male subjects to Delhi.13

In current study, 13.64% patients had history of a family member who had leprosy. In a study conducted by...
Thakkar et al only 8.3% cases had history of transmission from family member(s).14

Present study observed that the borderline lepromatous leprosy was the commonest type of leprosy with reaction (30%) followed by Borderline tuberculoid (26.36%), Lepromatous (21.82%), Tuberculoid (16.36%) and mid-borderline (5.55%) leprosy. Sharma, et al study in their study found that the borderline Tuberculoid type was the most commonest presentation of leprosy.13 Sallodkar and Kalla in their study conducted in Jodhpur, (Rajasthan) observed that the lepromatous leprosy was the most common group.15

Current study demonstrated that Type 1 reaction was present in 53.64% patients. The borderline tuberculoid leprosy type formed the major group (26.37%) with type 1 reaction. On the other hand, type 2 reaction was observed in 46.36% patients, wherein, borderline lepromatous leprosy constituted the major group (22.73%). Maximum type 1 reaction cases (33.90%) were observed between 3 to 6 months of anti-leprosy treatment whereas maximum cases of type 2 reaction (37.25%) were recorded between 6 to 9 months of undergoing anti-leprosy treatment.

Sharma et al study in their study reported type 1 and 2 reactions in 63.3% and 36.6% leprosy patients.13 In a similar study conducted by Sallodkar and Kalla study, among leprosy patients in Jodhpur Rajasthan, type 1 reaction was observed in 19.2% while type 2 reaction was seen in 80.1% cases.15

On studying duration of onset of reaction, Sharma et al in their study found that 51.6% (22/43) were newly diagnosed and had presented directly with reaction.13

Sallodkar and Kalla in their study reported that 33% of the patients had presented with type 1 reaction at their first visit15 while Brakel et al observed that 59% of suffered from type 1 reaction at the time of presentation.16 Current observation study found that 13.73% cases (7/51) of type 2 reaction were newly diagnosed. Sharma et al had reported 76.5% (19/25) cases with type 2 reaction at the time of presentation. Also, of 43 patients with type 1 reaction, 15 (34.80%) cases reported reactions within first 3 months whereas, 5 (11.60%) cases had type 1 reaction within 3 to 6 months and 1 (2.3%) case had reported reaction after completion of therapy. None of the patient showed type 1 reaction within 6 to 12 months of treatment while 1 (4%) case had type 2 reaction after 12 months of completion of therapy.13 In contrary, Manandhar et al observed that 34% of patients had type 2 reactions at time of presentation.17 Sharma et al out of the 43 patients with type 1 reaction, 32 (74.41%) had inflammation of previously existing lesions, 22 (53.6%) had concomitant neuritis, 5 (12.1%) had neuritis without any cutaneous lesions and 3 (7.31%) had edema of hands and feet.13

On analyzing reactions in this study, it was observed that the commonest presenting symptom associated with Type 1 reaction was 'inflammation of pre-existing lesion (59.32%). It was followed by neuritis (33.90% cases), new dermatological lesions (6.78% cases), neuritis with deformity (5.09% cases) and edema of hands and feet (10.17% cases) while the most common presenting feature of Type 2 reaction was ENL (66.67%) which was followed by bone pain (39.21%), neuritis (29.41%), neuritis with deformity (13.73%) and iritis (17.64%). Sharma et al (2004) found that of 25 patients presenting with type 2 reaction, 23/25 (92%) presented with papulonodular lesions, 10 (40%) had associated neuritis, and 2 (8%) suffered from periostitis. 1 case (4%) demonstrated eye involvement (iritis)15 while Manandhar et al reported neuritis and iritis in 20% and 5% cases, respectively.17

In present study, deformity rate of type 2 reaction (49.02%) was higher than Sharma et al study (28%). Deformity rate of type 1 reaction was lower (15.25%) than Sharma et al study (28%).13

In present study, feet were most common sites of disability (48.18%) and were followed by hands (43.64%) and eyes (1.82%). It was also observed that in type 1 reaction, hands were most common site of disability while in type 2 reaction, feet were found to be commonly affected. In contrast, Kalla and Sallodkar observed that hands were commonly disabled while feet, hands and eyes were seen to be affected in 37.78%, 42.22% & 13.33% of cases, respectively.15

Sarita et al (2013) reported that out of 34 patients with type 1 reaction, histopathological finding of upgrading reaction was detected in 47.06% cases while downgrading reaction was observed in 2.94% cases. In 17 cases (50%) biopsy reports were inconclusive. Also, from 14 patients, 8 (57.14%) patients had neutrophilic infiltration with macrophage granuloma and dural edema, only 1 (7.14%) case had neutrophilic vasculitis with macrophage granuloma and dural edema. In 5 cases (35.71%) of type 2 reaction, histopathological features were inconclusive.19

CONCLUSION

Leprosy related reactions are important as they can lead to significant morbidity. Disabilities and deformities due to reaction can lead social boycott of the patient because of fear & stigma. Although multi drug therapy has made the occurrence of lepra reactions less common, there are patients presented with reactions for the first time. Reactions do occur during multidrug treatment & even after release from treatment. This fact demands further efforts for prevention, early diagnosis, and appropriate management of reactions to prevent complications and disabilities.
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