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Original Article

A Clinico-epidemiological Profile of Lepra Reactions from a Tertiary Care Hospital in North India during 2016-2021

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Lepra reactions are acute exacerbations or chronic with or without recurrent episodes in silent course of leprosy which leads to complications thus requiring urgent medical attention and adjuvant treatment. As the profile of any disease and its complications may undergo variations from time to time in different settings this study has been undertaken to analyse recent clinico-epidemiological profile of lepra reactions in leprosy patients in a hospital setting. This was a retrospective, record-based study conducted on patients registered in the Hansen's disease clinic at our Tertiary Care Hospital of New Delhi from January 2016 to December 2021. Out of 169 patients treated during this period, 41(24.2%) developed reaction during course of the disease. Type 1 and 2 reaction was present in 32 (18.9%) and 9 (5.3 %)of patients respectively. Most common clinical presentation of type 1 reaction was cutaneous (increased redness, oedema, and tenderness of lesions) in 25/32 (78.1%), neuritis in 17/32 (53.12%). It was associated with facial and hands/feet edema in 4 (2+2)/32 (12.5%) of patients. Common factors associated with type 1 reaction were MDT initiation, borderline leprosy, age > 20 years, positive acid-fast bacilli (AFB) in smears, extensive disease (multiple cutaneous lesions, multiple nerve trunks) and facial involvement. In type 2 reaction, the most common presentation was cutaneous in 9/9 (100%), neuritis in 4/9 (55.5%), iridocyclitis 2/9 (22.2%) followed by epididymo-orchitis in 1/9 (11.1%) of patients. Most common morphologies of cutaneous lesions in Type 1 reaction were papulonodular in 44.4%, necrotic-ulcerative in 33.3% followed by papulopustular in 22.2% patients. Type 2 reaction showed an association with lepromatous leprosy, high bacteriological index (BI) >4+, preceding infection and stress. Majority of type 1 reaction was seen in BT leprosy (75%) followed by subpolar LL leprosy (LLs) (12.5%) while majority of type 2 reaction occurred in LL leprosy (77.7%) followed by BL (22.2%) leprosy. Active watchful approach should be exercised for prevention and early recognition of reactions and their predisposing factors. Timely appropriate management will minimise inflammatory damage and prevent consequences in the form of disabilities. As this is record based retrospective single centre study, it has limitations and these findings are indicative but may not be representative of situation at community level.

Keywords : Leprosy, Reactions, Profile, North India

Introduction

Leprosy also known as Hansen's disease is a chronic infectious disease which is caused by *Mycobacterium leprae*. It mainly affects skin and peripheral nerves (White & Franco-Parades 2015). It has been eliminated from India since December 2005 but new cases are still being reported annually implying ongoing transmission.

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According to World Health Organization (WHO) weekly epidemiological report of 2020, which mentions that out of 202,189 new cases reported globally, 114,451 (57%) were from India (WHO 2020). The term "reaction" is used to describe the appearance of symptoms and signs of acute inflammation in lesions of a leprosy patient. Two types of reactions affect 30% to 50% of patients: type 1 reaction (reversal reaction) and type 2 reaction (erythema nodosum leprosum [ENL]) (Meyerson 1996, Walker & Lockwood 2008). Type 1 reactions are commoner than type 2 reactions (Suchonwanit et al 2015). Type 1 reactions are delayed hypersensitivity reactions, characterised by increased inflammation of the pre-existing lesions, neuritis, neural dysfunction etc and these are the major cause of nerve function impairment (Nery et al 2013). The cutaneous manifestations of Type 2 reaction include superficial and deep erythematous, tender papules and nodules which heal with post inflammatory hyperpigmentation. Deformity assessment is a very relevant measure of leprosy control. According to global leprosy control strategy (2016-2020) by 2019, prevalence of grade 2 deformity was 1.4/ million population which was slightly higher than what was targeted (Sharma et al 2004).

In the last few decades, particularly with the advent of multi- drug therapy (MDT) and the use of anti-inflammatory therapies, there have been substantial improvements in long-term health outcomes for individuals diagnosed with leprosy. Although the worldwide prevalence of this disease has significantly decreased, leprosy is still a poorly understood illness, and often, the statistics do not capture the disability and dysfunction that remain after MDT is complete.

Materials and Methods

It was a record-based study conducted at our tertiary care hospital (Sucheta Kriplani Hospital) attached to Lady Hardinge Medical College, New Delhi, India. Records of all leprosy patients who attended leprosy clinic from January 2016 to December 2021 were analysed after receiving ethical clearance from institutional ethics committee (LHMC/IEC/2022/03/37). The patients with incomplete medical records were excluded from the study.

Methodology

Following methodology was followed:

- Records of patients diagnosed as leprosy and registered in the leprosy clinic during the above study period were analysed.
- Diagnosis of leprosy was confirmed on basis of clinical, histopathological findings and information pertaining to demographic data, clinical features, investigations including histopathology, treatment and complications were recorded on excel sheet from prefilled leprosy proforma.
- Ridley-Jopling classification (1966) was used for categorising patients into the following- polar tuberculoid (TT), borderline tuberculoid (BT), mid borderline (BB), borderline lepromatous (BL), polar lepromatous (LL) types. Pure neuritic leprosy was diagnosed according to IAL (1982) classification.
- Type 1 reactions were defined as acute exacerbation characterised by cutaneous lesions with redness and swelling, acute nerve tenderness with or without motor or sensory loss. It may be associated with oedema of face or hands and feet. Type 2 reactions were defined as multiple, tender, erythematous nodules/plaques with or without neuritis, constitutional symptoms/ involvement of other organs such as eyes, testes, joints, or bones.

- The operational definition of pauci-bacillary includes skin lesions of <5 associated with no nerve trunk involvement and smear negativity while multibacillary if 6 or more skins lesions, nerve trunk involvement and smear positivity for acid fast bacilli (NLEP 2013).

Results

Results of study are summarized in Tables 1 to 4.

Demographic details:

In our study subjects, out of 169 patients, 41(24.2%) presented with reactions, out of which 32(18.9 %) presented with type 1 reaction and 9(5.3%) presented with type 2 reaction (Table 1). Most of type 1 reactions- 13/32(40.6%) were seen in 30-40 years age group followed by 20-30 age group 8/32 (25%) while majority of type 2 reactions- 4/9 (44.4%) were seen in 20-30 years age group followed by 30-40 years age group. Type 1 reaction were equally seen in both male and female patients (50% in each gender type). Type 2 reaction were more commonly seen in male patients (66.7%) compared to females (33.3%) (p=0.46).

Clinical features of lepra reactions:

Most common clinical presentation among 32 cases with type 1 reaction was cutaneous in form of (increased redness, edema, tenderness) of lesions in 25(78.1%) followed by neuritis

Table 1 : Frequency of lepra reactions.

Lepra reaction	No.	%
Absent	128	75.7
Present	41	24.2
Type 1	32	18.9
Type 2	9	5.3

Table 2 : Clinical details of the patients in reaction.

S No	No of patients	%
TYPE 1 LEPRA REACTION		
Only cutaneous	11	34.37
Cutaneous + Hands/feet edema	2	6.25
Cutaneous + facial edema	2	6.25
Cutaneous + neural	10	31.25
Only neural	7	21.87
TYPE 2 LEPRA REACTION		
Only cutaneous	4	44.4
Cutaneous + Neuritis	2	22.2
Only neuritis	0	0
Cutaneous + neuritis + iridocyclitis	2	22.2
Cutaneous + neuritis + epididymorchitis	1	11.1

in 17(53.12 %) patients while both cutaneous and nerve involvement was present in 10 (31.25%). In type 2 reaction, cutaneous lesions were present in all patients 9 (100%). Most common morphology of cutaneous lesions was papulonodular in 4(44.4%) followed by necrotic-ulcerative (ulcers with necrotic base, irregular margins and eschar formation) in 3 (33.3%) followed by papulopustular (papules with overlying pustules and surrounding erythema) in 2(22.2%) patients.

In type 2 reactions, neuritis was seen in 5(55.5%) patients compared to 17(53.12%) in type 1 reaction. Majority (73.1%) of the patients in reaction developed nerve function impairment (NFI). Sensory NFI was seen in 24 (75%) patients in type 1 reaction and 6 (66.6%) patients in type 2 reaction. Both sensory and motor impairment was seen in 10 (31.2%) and 5(55.5%) in type 1 and 2 reactions respectively. In type 2 reaction, iridocyclitis was present in 22.2% patients followed by epididymo-orchitis in 11.1% patients (Table 2). Most of the Type 1 reactions (75%) were seen in BT leprosy whereas majority of Type 2 reaction (77.7%) were seen in LL leprosy (Table 3).

Relation with MDT and other triggering factors:

As is seen in Table 4, several patients initially presented with reactions only. Most of Type 1 reactions occurred during the treatment with multi-drug therapy, however, reactions occurred in a significant proportion of cases after MDT was completed.

Most type 1 reactions in our study, 20(62.5%) developed during the course of MDT, 7(21.8%) after the completion of treatment while 5(15.6%) presented at the onset of the disease whereas, 2/3rd (66.6%) of the patients presented with type 2 reactions at the first visit (Table 4). In type 1 lepra reactions, besides MDT other associations were - borderline classification in 27 (84.3%) patients, extensive disease (BT plaques involving ≥ 3 body segments) in 3(9.3%) patients and facial involvement in 2 (6.2%) patients.

Table 3 : Proportion of lepra reactions in different types of leprosy.

S No	Type I (n=32)	Type II (n=9)
TT (n=0)	0	0
BT (n=108)	24 (75%)	0
BB (n=1)	1 (2.3%)	0
BL (n=17)	2 (6.2%)	2 (22.2 %)
LL (n=29)	4 (12.5%)	7 (77.7%)
Pure neuritic (n=12)	1 (2.3%)	0
Histoid (n=2)	0	0

Table 4 : Onset of reaction in relation with MB-MDT.

S No	TYPE 1 (n = 32)	TYPE 2 (n=9)
At onset	5 (15.6%)	6 (66.6%)
During treatment with MB-MDT	20 (62.5%)	2 (22.2%)
Post treatment	7 (21.8%)	1 (11.1%)

In type 2 reaction, risk factors identified were LL leprosy in 7 patients, infections in 3, pregnancy in 2 and stress in 1 patient. In these patients with reactions slit skin smears were positive for acid fast bacilli (AFB) in 17 (41.4%) patients. In Type 1 reaction, AFB was seen in 8 (25.6%) patients while in Type 2 reaction, was present in all 9 (100%) patients.

Discussion

Leprosy has been eliminated from India as public health problem (prevalence less than 1/10,000 population at national level) since December 2005 but new cases are still being reported annually implying ongoing transmission. Reactions in leprosy are an immunological phenomenon that significantly impacts the course of the disease and associated disability. Frequency of reaction varies in different studies. In two Indian studies which were carried out prior to elimination of leprosy reaction was seen in 12.8% and 11% of patients (Salodkar & Kalla 1995, Sharma et al 2004). In our study, reaction was found in 24.2% of patients. Thomas et al. reported slightly higher frequency of 45 % compared to our study (Thomas et al 2017). In our study, majority of the reactions were seen in adult population (69.4 %) ranging from 30-40 years followed by 20-30 years age group (62.8%).

It is known that type 1 reaction or reversal reactions most commonly occur in border-line leprosy. Our data confirms the same during this period of 2016-2021. Existing skin lesions become erythematous and oedematous and may display ulcerative changes and may be accompanied by oedema of hands and feet (Goodless et al 1991). Reversal reaction is the leading cause of nerve damage in leprosy and may lead to permanent disability (WHO 2012). Reversal reaction is known to occur even years after MDT. The exact events that trigger reversal reaction are unknown. Risk factors for reversal reaction include increasing age (>20 years), postpartum period, bacteriological positivity (Kahawita et al 2008). In our study, type I reaction was seen in 18.9% of patients. Other studies on Type 1 reaction from India and abroad shows a prevalence ranging from 15% to 35% (Scollard et al 1994, Kumar et al 2004). In our study, most of patients were in 30-40 years age group and male and females were involved equally in type 1 reaction.

Most common clinical presentation of type 1 reaction was cutaneous 25 (78.1%) in form of increased erythema, oedema, and tenderness of lesions. Neuritis was present in 17 (53.1%) patients while 2 (6.25%) patients had hands/ feet and facial oedema each. Out of 32 patients in type 1 reaction, 11(34.3%) patients had cutaneous lesions only, 7(21.8%) patients had neuritis only while 10 (31.2%) had both cutaneous lesions and neuritis. (Table 2) Majority of type 1 reaction (62.5%) presented during the course of MDT; 15.6 % patients presented at onset of disease while 21.8% of patients presented after completing MDT. (Table 4) Similar clinical involvement was seen in another Indian study. Thomas et al (2017) reported slightly higher prevalence of type 1 reaction (32.5%) in their study. In their study, out of the 53 patients with type 1 reaction, 18 (33.9%) had only cutaneous lesions, 29 (54.7%) had only neuritis while 6 (11.3%) had involvement of both skin and peripheral nerves (Thomas et al 2017).

In our study, occurrence of type 1 reactions was associated borderline classification in 29 (90.2%) patients, initiation of MDT in 27 (84.3%) patients, extensive disease in 3(9.3%) patients and facial involvement in 2(6.2%) patients. Out of 32 patients in type 1 reaction, AFB was seen in 8(25%) of patients. Patients with bacteriological positivity can be considered as having increased risk of reaction.

Majority (75%) of type 1 reaction was seen in BT leprosy followed by 4(12.5%) in LLs leprosy followed by 2(6.25%) in BL leprosy followed by 1(3.1%) in BB leprosy and pure neuritic leprosy each (Table 3). Our results were similar to other studies in which they have reported higher frequency of type 1 reaction in BT leprosy followed by (LLs) leprosy (Chhabra et al 2015).

In our study, type 2 reaction were seen in 9 (5.3%) of patients. Thomas et al (2017) reported type 2 reaction in 12.3% in their study while in another Indian study, slightly lower frequency (4.3%) was noted (Sharma et al 2004). Majority of type 2 reaction occurred in 20–30-year age group and males were twice commonly involved compared to females. Our results were like another study in which males were more commonly involved in type 2 reaction. In another study, type 2 reaction was seen in 8.09% of patients (Thomas et al 2017). A systematic review reported the incidence of type 2 reactions to be between 0.7-4.6% of all the multibacillary cases (Voorend & Post 2013).

The reaction is marked by the rapid appearance of crops of painful, erythematous subcutaneous nodules that may ulcerate. Most common clinical presentation was cutaneous in all 9 patients. Most common morphological type was papulonodular followed by necrotic-ulcerative followed by papulopustular. Neuritis was present in 5 patients, 2 patients presented with iridocyclitis while 1 had epididymo-orchitis. In the study by Thomas et al (2017) among 20 patients who developed type 2 reaction, 13 developed nodular lesions and 7 developed neuritis and nodular skin lesions.

ENL can happen any time during the course of leprosy but is most common within 1 year of starting MDT. In our study also, majority 6 (66.6%) of patient presented with type 2 reaction at onset, 2 (22.2%) during treatment while 1(11.1%) presented after treatment. Risk factors for ENL include lepromatous leprosy or borderline lepromatous disease with high bacterial load (Manandhar et al 1999). Other less well-defined risk factors include pregnancy, lactation, puberty, intercurrent infection, vaccination, and stress (Manandhar et al 1999). Factors associated with type 2 reactions were >4+ BI in 7 patients of LL leprosy and 2 patients of BL leprosy, infections (bacterial and viral) in 3 patients and stress in 1 patients. In LL leprosy, type 2 reaction occurred in 7 patients, in BL leprosy, 2 had reaction. These findings are similar to those of Pocaterra et al who reported that type 2 reaction were seen in 50% of LL patients and 5-10% of BL patients (Pocaterra et al 2006).

Conclusions

In this study, the prevalence of lepra reactions was 24.2%. Type 1 and type 2 reactions were seen in 18.9 and 5.3% of the patients respectively. The risk factors associated with the development of type 1 reactions were age >20 years, positive bacteriological Index, MDT therapy, extensive disease, borderline leprosy, and facial involvement. The risk factors in type 2 reactions identified were male sex, lepromatous leprosy, high bacterial load, stress, and infections. Patients at higher risk of reaction and after initiation of MDT were followed more frequently, any concurrent infections were treated. Early initiation of steroids was beneficial in reducing severity of reactions and prevention of deformity. While these associated/ triggering factors have been known for a long time, it is important to understand their current roles so that treating doctors remain alert about recent trends.

It would be important to identify these reactional states and active watchful approach should be exercised for early recognition of reactions and institute treatment which will minimise

inflammatory damage. Closer monitoring of patients at higher risk would help in minimising their occurrence and timely management.

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