Section: Skin and VD

Original Research Article

A CLINICO EPIDEMIOLOGICAL STUDY ON REACTIONS IN LEPROSY: A CROSS-SECTIONAL STUDY FROM A TERTIARY CARE HOSPITAL IN EASTERN INDIA

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Abstract

Background: Leprosy is a chronic, infectious, granulomatous disease caused by Mycobacterium leprae. It mainly affects the cooler areas of the body, notably the skin and peripheral nerves. Its diagnosis is established based on the clinical, neurological, slit-skin smear and histopathological examination of the patient. The term leprosy is a tribute to the Norwegian physician Gerhard Armauer Hansen, who identified the bacillus Mycobacterium leprae as the cause Leprosy patients continue to present in many countries and will need proper diagnosis and treatment, and proper counseling of patients along with suitable rehabilitation programmes. **Materials and Methods:** It was a record-based study conducted at our tertiary care hospital (Patna Medical College and Hospital, Patna, Bihar). Records of all leprosy patients who attended leprosy ward from September 2017 to August 2021 were analyzed after receiving ethical clearance from institutional ethics committee. The patients with incomplete medical records were excluded from the study. **Result:** In our study subjects, out of 100 patients, 25(25%) presented with reactions, out of which 20(20%) presented with type 1 reaction and 5(5%) presented with type 2 reaction (Table 1). Most of type 1 reactions were seen in 30-40 years age group followed by 20-30 age groups while majority of type 2 reactions were seen in 20-30 years age group followed by 30-40 years age group. Type 1 reaction was equally seen in both male and female patients (50% in each gender type). Type 2 reaction was more commonly seen in male patients (75%) compared to females (25%). **Conclusion:** Our study, we can infer that leprosy is still prevalent in our community, in children as well, indicating community transmission, and therefore we propose further skill development and training in prompt diagnosis and management of this disease.

INTRODUCTION

Leprosy is a chronic, infectious, granulomatous disease caused by Mycobacterium leprae. It mainly affects the cooler areas of the body, notably the skin and peripheral nerves. Its diagnosis is established based on the clinical, neurological, slit-skin smear and histopathological examination of the patient. The term leprosy is a tribute to the Norwegian physician Gerhard Armauer Hansen, who identified the bacillus Mycobacterium leprae as the cause of the disease in 1873.[1] M. leprae is a straight or slightly curved rod shaped bacillus, with rounded ends, measuring 1.8-5 microns in length and 0.2-0.5 microns in diameter. In smears, it is red stained with fuchsin using the Ziehl-Neelsen stain and because of its high lipid content, it does not get discoloured when washed with alcohol and acid, thus being acid-fast bacilli. When Gram staining is used, M. leprae is gram-invisible, appearing as negatively stained images, called ghosts, or as bead like Gram positive bacilli.[2,3] M. leprae mainly infects macrophages and Schwann cells. It has never been grown in artificial media. It remains viable for days in the environment.[2-6,9] The main route of transmission is the nasal mucosa.[7,8] Less commonly, it can occur by skin erosions.[8,9] Other transmission routes, such as blood, vertical transmission, breast milk, and insect bites are also possible. Three cardinal signs have remained the basis for the basis of clinical diagnosis of leprosy.[10] Anaesthetic/ hypoanaesthetic skin lesion(s), Thickened peripheral nerve(s) with impairment of sensations in the area supplied, Acid-fast bacilli in the skin smear.

The classification system of Ridley and Jopling uses the concept of spectral leprosy based on clinical, immunological and histopathological criteria.[11,12] The borderline form is divided into borderline

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tuberculoid (BT), borderline lepromatous (BL) and mid-borderline (BB) forms. Leprosy reactions result from changes in the immune balance between the host and M.leprae. These are acute episodes that primarily affect the skin and nerves, also having systemic manifestations like fever, joint pain, nausea, vomiting, abdominal pain etc. They may occur during the natural course of the disease, throughout treatment or after it. They are classified into 2 types- Type 1 and 2 reactions.[13,14] In type 1, also called as reversal reaction, there is Erythema, inflammation and tenderness in the existing leprosy lesions along with systemic symptoms like fever, joint pain etc. in type 2 reaction, also called as Erythema Nodosum Leprosum, there is appearance of crops of reddish, tender papules, nodules and plaques all over the body which may present with some unique systemic features like ocular and testicular inflammation. WHO proposed an MDT (Multidrug therapy) for the treatment of leprosy.[15] The first line drugs are rifampicin, dapsone and clofazimine. In paucibacillary cases, it is given for 6 months while in multibacillary cases, it is for 12 months.

Relapsed multibacillary patients are also retreated with triple therapy regardless of any change in classification.[16] Several new drugs bactericidal for M. leprae have been identified- fluoroquinolones, minocycline and clarithromycin. Treatment of reactions is aimed at controlling acute inflammation, easing pain, reversing nerve and eye damage and reassuring the patient. MDT should be continued. Neuritis or moderately inflamed skin lesions should be treated with corticosteroids. Standardized courses of prednisolone have been used, starting at 40mg daily, reducing by 5mg every 2-4 weeks.[17] Erythema nodosum leprosum is a difficult condition of treat, and frequently requires therapy with high dose steroids (80mg daily, tapered down rapidly) or thalidomide. Thalidomide 400mg daily is superior to steroids in controlling ENL, and is the drug of choice for young men with severe ENL.[18]

Lastly, complete rest is very crucial for effective cure of all lepra reactions. There was a WHO-led campaign to eliminate leprosy as a public health problem. Although this focuses resources and energy on leprosy, the effect of a target-driven approach was eventually counterproductive.[19] Many vaccines have also been developed for leprosy like the BCG vaccine, Mycobacterium indicus pranii (MIP) or Mycobacterium w, Indian Cancer Research Centre (ICRC) Bacillus, Mycobacterium vaccae, Mycobacterium habana, purified recombinant antigens etc. Leprosy patients continue to present in many countries and will need proper diagnosis and treatment, and proper counseling of patients along with suitable rehabilitation programmes.

MATERIALS AND METHODS

It was a record-based study conducted at our tertiary care hospital (Patna Medical College and Hospital, Patna, Bihar). Records of all leprosy patients who attended leprosy ward from September 2017 to August 2021 were analyzed after receiving ethical clearance from institutional ethics committee. The patients with incomplete medical records were excluded from the study.

Records of patients diagnosed as leprosy and registered in the leprosy Ward during the above study period were analyzed. 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 characterized 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

In our study subjects, out of 100 patients, 25(25%) presented with reactions, out of which 20(20%) presented with type 1 reaction and 5(5%) presented with type 2 reaction [Table 1]. Most of type 1 reactions were seen in 30-40 years age group followed by 20-30 age groups while majority of type 2 reactions were seen in 20-30 years age group followed by 30-40 years age group. Type 1 reaction was equally seen in both male and female patients (50% in each gender type). Type 2 reaction was more commonly seen in male patients (75%) compared to females (25%).

Most common clinical presentation among 20 cases with type 1 reaction was cutaneous in form of (increased redness, edema, tenderness) of lesions in 75(75%) followed by neuritis in 55(55 %) patients while both cutaneous and nerve involvement was present in 30(30%). In type 2 reaction, cutaneous lesions were present in all patients 5 (100%). Most common morphology of cutaneous lesions was papulonodular in 3(60%) followed by necrotic-ulcerative (ulcers with necrotic base, irregular margins and eschar formation) in 1 (20%) followed by papulopustular (papules with overlying pustules and surrounding erythema) in 1(20%) patients.

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In type 2 reactions, neuritis was seen in 2(50.5%) patients compared to 110(50%) in type 1 reaction. Majority (75%%) of the patients in reaction developed nerve function impairment (NFI). Sensory NFI was seen in 15 (75%) patients in type 1 reaction and 12 (60%) patients in type 2 reaction. Both sensory and motor impairment was seen in 6 (30%) and 3(50.5%) in type 1 and 2 reactions respectively. In type 2 reaction, iridocyclitis was present in 25% patients followed by epididymo-orchitis in 12% patient. Most of the Type 1 reactions (75%) were seen in BT leprosy whereas majority of Type 2 reaction (80%) were seen in LL leprosy.

As is seen in [Table 3], 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, 12(60%) developed during the course of MDT, 5(25%) after the completion of treatment while 3(20%) presented at the onset of the disease whereas, 2/3rd (70%) of the patients presented with type 2 reactions at the first visit [Table 3]. In type 1 lepra reactions, besides MDT other associations were - borderline classification in 17 (85%) patients, extensive disease (BT plaques involving ≥ 3 body segments) in 2(10%) patients and facial involvement in 1 (5%) patients.

In type 2 reaction, risk factors identified were LL leprosy in 2patients, infections in 1, pregnancy in 1 and stress in 1 patient. In these patients with reactions slit skin smears were positive for acid fast bacilli (AFB) in 8 (40%) patients. In Type 1 reaction, AFB was seen in 5 (25.%) patients while in Type 2 reaction, was present in all 5 (100%) patients.

Table 1: Frequency of lepra reactions.

Lepra Reaction	No.	%
Abscent	70	70
Present	25	25
Type 1	20	20
Type 2	5	5

Table 2: Clinical details of the patients in reaction.

SN.	N0. Of Patient	%
Type 1 Lepra Reaction		
Only cutaneous	7	35
Cutaneous + Hands/feet edema	2	10
Cutaneous + facial edema	2	10
Cutaneous + neural	6	30
Only neural	3	15
Type 1 Lepra Reaction		
Only cutaneous	4	80
Cutaneous + Neuritis	1	20
Only neuritis	0	0
Cutaneous + neuritis + iridocyclitis	0	0
Cutaneous + neuritis + epididymorchitis	0	0

Table 3: Onset of reaction in relation with MB-MDT.

SN.	Type 1	Type 2
At onset	3 (15%)	3 (60%)
During treatment with MB-MDT	12(60%)	1(20%)
Post treatment	5(25%)	19(20%)

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).[20] In our study, reaction was found in 25% 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 (70 %) ranging from 30-40 years followed by 20-30 years age group (65%).

It is known that type 1 reaction or reversal reactions most commonly occur in border-line leprosy. Our data confirms the same during my study period. 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).[21] In our study, type I reaction was seen in 20% of patients. Other studies on Type 1 reaction from India and abroad shows a

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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 among 20 cases with type 1 reaction was cutaneous in form of (increased redness, edema, tenderness) of lesions in 75(75%) followed by neuritis in 55(55 %) patients while both cutaneous and nerve involvement was present in 30(30%). In type 2 reaction, cutaneous lesions were present in all patients 5 (100%). Most common morphology of cutaneous lesions was papulonodular in 3(60%) followed by necrotic-ulcerative (ulcers with necrotic base, irregular margins and eschar formation) in 1 (20%) followed by papulopustular (papules with overlying pustules and surrounding erythema) in 1(20%) patients. In type 2 reactions, neuritis was seen in 2(50.5%) patients compared to 110(50%) in type 1 reaction. Majority (75%%) of the patients in reaction developed nerve function impairment (NFI). Sensory NFI was seen in 15 (75%) patients in type 1 reaction and 12 (60%) patients in type 2 reaction. Both sensory and motor impairment was seen in 6 (30%) and 3(50.5%) in type 1 and 2 reactions respectively. In type 2 reaction, iridocyclitis was present in 25% patients followed by epididymo-orchitis in 12% patient. Most of the Type 1 reactions (75%) were seen in BT leprosy whereas majority of Type 2 reaction (80%) were seen in LL leprosy. 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).[22]

As is seen in [Table 3], 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, 12(60%) developed during the course of MDT, 5(25%) after the completion of treatment while 3(20%) presented at the onset of the disease whereas, 2/3rd (70%) of the patients presented with type 2 reactions at the first visit [Table 3]. In type 1 lepra reactions, besides MDT other associations were - borderline classification in 17 (85%) patients, extensive disease (BT plaques involving ≥ 3 body segments) in 2(10%) patients and facial involvement in 1 (5%) patients. 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).[23]

In our study, type 2 reaction were seen in 5(5%) 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).[24] 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 5 patients. Most common morphological type was papulonodular followed by necrotic-ulcerative followed by papulopustular. 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. 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).[25] 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).

CONCLUSION

Leprosy is a chronic, infectious disease that presents with a wide range of clinical manifestations ranging from various morphological skin lesions, nerve function impairment-both sensory and motor, deformities like clawing of digits, trophic ulcer and foot/wrist drop. There is also the development of leprosy reactions which result in fever, systemic upset, higher chances of nerve function impairment and deformities. Though Hansen has lower rate of mortality, its high level of morbidity and decrease in quality of life of the patient cannot be underestimated. In our study, majority of the patients belonged to the middle age and older age group and less patients in the children and adolescent group, this signifies that Hansen has a long incubation period which is the cause, it is not that much evident in children. However, the high incidence in children signifies higher rate of infection in the community. Though most of the patients belonged to rural areas, a moderate proportion of them belonged to the urban areas as well. Although most of the patients belonged

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to the lower socio-economic strata, a considerable number of patients were found in the middle-income group and a few patients in the higher income group. This proves the fact that Hansen cannot be ruled out in the middle or higher socio-economic group. A number of patients have completed their higher secondary education and few of them were even graduates. People in the higher socio-economic strata often feel embarrassed or anxious to visit the doctor in case of Hansen due to the social stigma associated with it. This can often result in delay in diagnosis and institution of treatment. Hansen has a huge burden of disabilities and deformities. It can add to considerable morbidity in the life of a person. It is important both for the patient and the doctor to take proper care of these disabilities and rehabilitation also forms an important part so that the patient can find alternative occupation and means of livelihood. In our study, too, we have seen patients presenting with various deformities like clawing of digits, foot drop, wrist drop, trophic ulcers etc. Thus, from our study, we can infer that leprosy is still prevalent in our community, in children as well, indicating community transmission, and therefore we propose further skill development and training in prompt diagnosis and management of this disease.

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