International Journal of Research in Dermatology
Nataraj P et al. Int J Res Dermatol. 2018 Nov;4(4):527-533
http://www.ijord.com

DOI: http://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20184455

Original Research Article

A clinical, epidemiological and histopathological study of leprosy reactions

Perumalla Nataraj, Komeravelli Haritha*

Department of Dermatology, Venereology and Leprosy, RVM Institute of Medical Sciences and Research Centre, Mulugu Mandal, Siddipet, Telangana, India

Received: 11 July 2018
Revised: 27 August 2018
Accepted: 28 August 2018

***Correspondence:**
Dr. Komeravelli Haritha,
E-mail: haritha_komeravelli@yahoo.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Leprosy reactions are acute emergencies in the otherwise generally indolent course of leprosy. The present study was done to know the epidemiology, clinical manifestations and its histopathological findings..
Methods: A total of 50 patients attending out patient, in the department of Dermatology, venereology and Leprosy at Chigateri Hospital and Bapuji Hospital were included. Detailed history, thorough physical examination and relevant investigations were done.
Results: Out of all leprosy outpatients, reactions constituted 16.8%. 66% patients belonged to age group of 21-50 years, with a male to female ratio of 1.94:1. The disease was more common among the illiterates (80%), coolies (52%) and low socio-economic status (76%). Type I (RR) reaction (66%) and Type II (ENL) reaction (34%) which, commonly presented during 1st year of MDT and 2 years of MDT respectively. Borderline spectrum (74%), Anti-leprosy drugs (46%) were major risk factors associated. Erythematous, edematous skin lesions (50.6%); erythematous tender nodules (100%) along with neuritis were most common clinical features in Type I (RR) and Type II (ENL) reactions respectively. Edema (63.6%), lymphocytes (60.6%) and epitheloid cells (54.5%) were major histopathological findings in Type I (RR) reaction where as vasculitis (100%), increased vascularity (82.3%) and PMNL cells (88.2%) in Type II (ENL) reaction.
Conclusions: This study emphasizes the need for detailed history, clinical examination and investigations including biopsy for timely recognition of reactions, in order to halt the progress and prevent the permanent damage it causes.

Keywords: Reversal reaction, Erythema nodosum leprosum

INTRODUCTION

Mycobacterium leprae causes leprosy. In some cases it may be infectious to others. It affects mainly the nerves, and the skin. In fact it can affect any body part. Culture is difficult inspite the fact that the organism was discovered for more 100 years ago.[1]

Many factors, such as active participation of the missionaries, movements of population from rural areas to urban areas and country to country, overcrowding, poverty, malnutrition, inadequate and untimely treatment accentuate the prevalence of the disease.[2,3]

Leprosy is a chronic actively progressing disease and during its long course, there may occur acute bouts of exacerbation, generally called as 'reactions'. The occurrence of such reactive episodes in lepromatous and Borderline are detrimental to the patient, since these results in deterioration of his clinical condition and setting up of new foci of activity of the disease. They sometimes interfere with the specific treatment and

dampen the spirits of the patients and the physicians alike. Female gender, wide spread disease, multi-bacillary disease, immunosuppression, HIV, pregnancy and lactation are identified as risk factors and sometimes no obvious reasons can be detected for the rapid transformation to the reactional state.[4]

Reactions in leprosy are classified into type-1 reaction, type-2 reaction and Lucio phenomenon or type-3 reaction. Type-1 reaction is characterized by erythema, edema of the skin lesions, macules become plaques or develop raised edges. It is associated with a change in CMI and is seen mostly in BT patients. It fits into Gell and Coombs type IV reactions. Along with skin manifestations, neuritis and edema of hands and feet is common. Type-2 reaction is also known as lepromatous lepra reactions which presents with small, 2-5 mm, papules or larger nodules which are painful and tender to touch. ENL is only skin manifestation. Neuritis, iridocyclitis, orchitis, is other systemic manifestations seen. This commonly occurs in LL patients and to some extent in BL patients. This fits into Gell and Coombs type-3 reactions which are humoral or immune complex mediated. Type-3 reaction or Lucio phenomenon is characterized by necrotizing lesions, which may go on to extensive ulceration of skin. First it was described in Mexican patients. Histopathological changes are not diagnostic of leprosy reactions but if clinically correlated it helps in the diagnosis and follow up.[5]

The present study was done to know the epidemiology, clinical manifestations and its histopathological findings.

METHODS

The study group was drawn from patients attending the outpatient and inpatient, Department of DVL at Chigateri General Hospital and Bapuji Hospital, attached to JJM Medical College, Davangere for a period of 2 years from October 2005 to September 2007.

50 patients were selected as per inclusion and exclusion criteria.

Inclusion criteria

Inclusion criteria were Proven cases of leprosy histopathologically; patients who came with reactions for first time.

Exclusion criteria

Exclusion criteria were patients without previous histopathological report and who do not give consent for biopsy; pregnant women.

A detailed history was taken. A detailed general examination was carried out. Local examination was carried out. In every patient, the extent of nerve involvement was noted – whether a single nerve or multiple nerves.

All the systems were carefully examined and systemic involvement if any was noted down. All the cases that were clinically and provisionally diagnosed as cases of reactions in leprosy were investigated as follows. All the patients diagnosed were investigated routinely

Slit smear examination

Skin smear examinations was carried out by taking a slit and then scrape the skin from five sites like two from ear lobes, two from eyebrows and one from existing active lesion.

The bacteriological index (BI) and the morphological index (MI) were calculated according to Ridley's scale.

The morphological index

It is the percentage of solid stained bacilli. This was calculated after examining 200 red staining elements lying singly.

Biopsy

Biopsy was taken and tissue was preserved in 10% formalin before it was processed for histopathological study at the histopathology department. The sections were stained routinely with the haematoxylin and Eosin procedure.

Statistical analysis

The data was entered in the Microsoft Excel worksheet and analyzed using proportions.

RESULTS

Majority i.e. 14 patients (28%) belonged to age group of 21-30 years. The overall incidence among males and females is 66% and 34% respectively. 38 cases (76%) belong to the lower socio economic status. 52% of the cases belong to Labourers. almost three fourth (72%) of the patients were illiterate. 40 patients (80%) belong to the rural area (Table 1).

2/3rd of patients had type-I reactions i.e. 66%, were as 1/3rd of patients i.e. 34% had type-II reaction (Table 2).

Among the 33 patients who had type I reaction, 28 patients (56%) were Borderline tuberculoid, 3 (6%) were mid borderline and 2 (4%) were borderline lepromatous. Only 17 patients (out of 50) had type II reactions out of which 4 (8%) were of borderline lepromatous leprosy and 13 (26%) were of lepromatous leprosy (Table 3).

Anti-leprosy drugs constitute the major risk factor (48%) and physiological stress (menstruation), physical strain, psychological stress, extremes of climate (summer), concomitant infection and idiopathic constitute the other (52%) (Table 4).

Erythema and swelling of the skin lesions were present in 50.6% of the cases, occurrence of new skin lesions in 24.2%, Neuritis in 39.3%, neuritis and skin lesions in 21.2%, fever in 18.1% and edema of hands and feet in 30.3% of the total 33 (100%) of type I reaction cases. No case of ulceration was noted (Table 5).

All the 17 patients (100%) presented with fresh crops of tender nodules. Joint pain, neuritis, ulceration and edema (88.2%), myalgia (82.1%), fever (76.4%) were the next common clinical features. Iritis (11.7%) orchitis (35.2%) and lymphadenopathy (17.1%) were the least features encountered (Table 6).

Among the patients who presented with type I reaction 10 patients (20%) were seen with a reaction during the first visit, 20 patients (40%) developed the reaction during the first year after diagnosis. Out of 17 patients who had type II reaction, one patient had reaction at the first visit, 4 patients (8%) had during the first year (Table 7).

Table 1: Distribution of study subjects as per socio-demographic characteristics.

Socio-demographic characteristics		Number	%
Age (in years)	11-20	8	16
	21-30	14	28
	31-40	8	16
	41-50	11	22
	51-60	6	12
	>60	3	6
Sex	Male	33	66
	Female	17	34
Social class	Middle	12	24
	Lower	38	76
Occupation	Agriculture	7	14
	Housewives	2	4
	Baggers	3	6
	Labourers	26	52
	Students	4	8
	Professionals	8	16
Education status	Illiterate	36	72
	Literate	14	28
Residence	Rural	40	80
	Urban	10	20

Table 2: Distribution of study subjects as per type of reaction.

Type of lepra reaction	Number	%
Type I	33	66
Type II	17	34
Total	50	100

Table 3: Reactions in different types of leprosy.

Type of leprosy	Type of lepra reaction				Total	
	Type I		Type II			
	Number	%	Number	%	Number	%
TT	0	0	0	0	0	0
BT	28	56	0	0	28	56
BB	3	6	0	0	3	6
BL	2	4	4	8	6	12
LL	0	0	13	26	13	26
ID	0	0	0	0	0	0
Total	33	66	17	34	50	100

Table 4: Precipitating factors of lepra reactions.

Precipitating factors	Number	%
Physiological stress (menstruation)	3	6
Anti-leprosy drugs	24	48
Physical strain	8	16
Psychological stress	5	10
Extremes of climate	6	12
Not known	4	8
Total	50	100

Table 5: Clinical features of type I reactions.

Clinical features	Number	%
Erythema and swelling skin lesions	20	50.6
New skin lesions	8	24.2
Edema hands and feet	10	30.3
Ulceration	0	0
Neuritis and skin lesions	7	21.2
Neuritis alone	13	39.3
Fever	6	18.1

Table 6: Clinical features of type II reactions.

Clinical features	Number	%
Fresh crops of erythematous and tender nodules	17	100
Fever	13	76.4
Joint pain, neuritis, edema and ulceration	15	88.2
Iritis	2	11.7
Orchitis	6	35.2
Lymphadenopathy	3	17.1
Myalgia	14	82.1

Table 7: Time of reactions.

Type of reaction	Timing of reactions	Number	%
Type I	At diagnosis	10	20
	During first year	20	40
	During second year	3	6
Type II	At diagnosis	1	2
	During first year	4	8
	During second year	6	12
	During third year	6	12
Total		50	100

Table 8: Recurrence of reactions.

Type of reaction	Single episode		Multiple episodes	
	Number	%	Number	%
Type I	24	72.7	9	27.3
Type II	04	23.6	13	76.7

Out of 33 patients with type I reaction 24 (72.7%) had one episode and 9 patients (27.3%) had multiple episodes of type I reaction during the period of 2 years. Among patients who had type II reactions 4 patients (23.6%) had only one episode and 13 patients (76.4%) had multiple episodes during the same period (Table 8).

Among patients of type I reaction edema of the dermis, infiltration by lymphocytes and epitheloid cells were more commonly seen. Few specimens showed giant cells and macrophages. Among the specimens taken from patients of type II reaction vasculitis was seen in all the patients, infiltration by PMNL in 88.24%, increased vascularity in 82.35% and edema in 58.82% (Table 9).

Table 9: Histopathology of skin smears.

Type of reaction	Features	Number	%
Type I	Edema	21	63.63
	Lymphocytes	20	60.6
	Epitheloid cells	18	54.55
	Giant cells	4	12.12
	Macrophages	2	6.06
Type II	PMNL cells	15	88.24
	Edema	10	58.82
	Increased vascularity	14	82.35
	Vasculitis	17	100

DISCUSSION

Out of 1685 patients attending the skin and leprosy Department, 284 patients (16.8%) were found to have reactions. Out of which type I reactions constituted 11.3% and type II reactions 5.5%. Kumaran et al reported incidence of type I reactions as 2.6% to 28% and type II reaction as 2.1% to 47.4%. The present study is in concurrence with the above mentioned study.[6]

In the present study 28% belonged to age group of 21-30 years. There were only 8 patients (16%) who were below 20 years. Scollard et al found that 17% belonged to the age group below 20 years. But this study group consisted of only patients who presented with type II reactions. The same authors in the study of 81 patients of Type-I reaction found more patients in the age group of 21 years and above there were 19 patients (23.4%). Thus the age incidence on an average is 20%.[7]

In the present both type-I and type-II reactions were more common in men than in women. Kumaran et al found an incidence of 60% among males and 40% among females which included both type-I and type-II reactions.[6] However Scollard et al had observed higher incidence of type-I reaction among females a 47% but the overall incidence of reactions i.e., both type-I and type-II reactions was 26%.[7]

In the present study 76% belonged to the low income group. There were none in the high income group. Ponnighaus et al reported more cases from low social classes.[8] Jopling et al had observed that poor housing conditions and poor nutrition are important factors in the spread of leprosy.[2] In the present study it is quite evident, because more number of patients belonged to the lower socio-economic status, hence the incidence of reactional leprosy was more among patients belonging to lower socio-economic status.

In the present study majority were labourers, where as the agriculturists, professional, housewives, students and others contributed to the rest (48%). There are no available studies to compare the occupational status with particular references to reactional leprosy.

In the present study 72% of the patients were illiterate and even among the remaining (28%) the literacy level was low. Jopling et al observed that leprosy is the thermometer of civilization which depends upon the literacy and economic status of the persons.[2]

80% of patients were from rural area in the present study. Ponnighaus et al found higher incidence of leprosy among rural areas which was attributed to poor housing status, poor educational status, poverty and malnourishment which are of great epidemiological significance.[8]

In the present study 66% of patients had type-I reaction whereas 34% of patients had type-II reaction. Kumaran VP et al noted that 71.5% had type-I reaction whereas 28.5% had type- II reaction.[6] Scollard et al found type-I reaction in (64.1%) and type-II reaction (35.9%) of the patients.[7]

Among the 33 patients who had type I reaction, 28 patients were Borderline tuberculoid, 3 were mid borderline and 2 were borderline lepromatous. Thus borderline tuberculoid patients had higher incidence of type I reaction. Out of 17 patients who had type II reactions, 4 were of borderline lepromatous leprosy and 13 were of lepromatous leprosy. Desikan et al noted that out of 412, 313 had BT, 9 had BB, 85 had BL and 5 had LL.[9] Among 95 patients who had type II reaction 61 had LL and 34 had BL. Sehgal et al found that out of 22 patients who presented with reaction 11 were of type I (BT-6, BB-1, BL-4) and 11 patients were type II reaction and all the patients belong to LL spectrum.[10]

In the present study anti-leprosy drugs constituted the major risk factor (48%). Kumaran et al found female gender, disseminated disease, physiological stress, multi-bacillary leprosy were the major risk factors.[6] Nigam et al mentioned that 64.5% of their patients developed reactions during dapsone therapy.[11]

50.6% of the cases were found to have erythema and swelling of the skin lesions in the present study. No case of ulceration was noted. Lockwood et al noted that incidence of skin lesions alone was 43.1%, Both skin lesions and neuritis was seen in 22.7% and only neuritis without any ulceration was noted in 31.8% of the patients.[12] Pfaltzgraff et al stated that type I reactions are characterized by "erythema and swelling of the existing

lesion and neuritis".[13] This has been mentioned by Jopling et al also.[14]

In the present study 100% presented with fresh crops of erythematous and tender nodules. Van Brakel et al study showed presence of clinical signs is diagnostic of ENL i.e., multiple, usually small, tender nodules, with or without ulceration, neuritis (shooting or burning), fever, edema, involvement of other organs, e.g., Iritis, orchitis and arthritis.[15] Pfaltzgraff et al and Jopling et al also mention the same features for ENL reaction.[13,14]

20% of the patients with type I reaction developed the reaction while in the first visit. Around 40% developed reaction in the first year of diagnosis. Out of 17 patients who had type II reaction, one patient had reaction at the first visit, 8% had during the first year, 12% had during the second year and another 12% had the reaction after two years. Kumaran et al also reported similar findings.[6]

In the present study 72.7% had a one episode and 27.3% had multiple episodes of type I reaction during the period of 2 years. Among patients who had type II reactions 23.6% had only one episode and 76.4% had multiple episodes during the same period. Ponnighaus et al found that 68.58% had one episode and 31.42% had multiple episodes.[8] Kumaran et al noted that 70.6% had single episode of recurrence and 29.4% had 2 or more episodes among patients of type I reaction. Among patients of type II reaction 12.1% patients had single episode, 64.4% up-to 4 episodes and 23.5% had 4 or more than 4 episodes.[6]

In the present study among patients of type I reaction edema of the dermis, infiltration by lymphocytes and epitheloid cells were more commonly seen. Few specimens showed giant cells and macrophages. Among the specimens taken from patients of type II reaction vasculitis was seen in all the patients, Infiltration by PMNL in 88.24% increased vascularity in 82.35% and edema in 58.82%. Radia et al found epitheloid cells predominantly in type I upgrading reactions and more macrophages in type I downgrading reactions.[16] Lucas et al have described predominance of lymphocytes in type I upgrading reactions and in type II reactions they have described neutrophilic predominance, vasculitis and occasionally eosinophils.[17] Job describes "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 in upgrading type I reaction".[18]

In the present study of 50 patients skin biopsy was done and sent for histopathology. 33 (66%) of the patients were proved type I reaction and 17 (34%) of the patients were proved type II (ENL) reaction. In the study of Sehgal et al out of 22 patients, 11 (50%) were histopathologically proved of Type I reaction and 11 (50%) patients were of type II (ENL) reaction.[10] The present study has slight higher incidence of type-I reaction.

CONCLUSION

As majority of the patients had borderline leprosy which is the usual scenario, type I reaction was more among them. Similarly the higher incidence of type II reaction among LL patients is an established fact. Anti-leprosy drugs were the commonest precipitating factor as seen in majority of studies, which should be explained to the patient. Otherwise there is a tendency among these patients to stop these drugs. The occurrence of type I reaction during first year of treatment and that of type II after 2 years is an established fact. With regard to the recurrences single episode was more common in type I reaction and multiple episodes in type II reaction. The reactions clinically can be well correlated by histopathology. Although histopathology is not diagnostic, when clinically correlated is a useful tool which aid in the diagnosis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Dharmendra. History of spread and decline of leprosy. Leprosy. Vol. I, Kothari Medical Publishing House, Bombay; 1978: 7-21.
2. Jopling WH, Mcdougall AC. Definition Epidemiology and World distribution. The handbook of leprosy. 5th ed. CBS Publishers and Distributors, New Delhi; 1996: 1-9.
3. Rastogi N, Rastogi RC. Leprosy in ancient India. Int J Lepr. 1984;52:541-3.
4. Ebbel B. A contribution to the earliest history of leprosy. Int J Lepr. 1935;3:257.
5. Noordeen SK. The Epidemiology of leprosy. In: Hastings RC, editor. Leprosy. 2nd ed. Edinburgh London Madrid Melbourne New York and Tokyo: Churchill Livingstone; 1994: 3-10.
6. Kumaran VP, Manimozhi N, Jesudasan Kumar. Incidence of late lepra reaction among multi-bacillary leprosy patients after MDT. Int J Lepr other mycobact Dis. 1995;63(1):18-22.
7. Scollard DM, Smith T, Bhoopath L, Theetranont C, Rangdaeng S, Morens DM. Epidemiologic characteristic of leprosy reactions. Int J Lepr. 1994;62(4):559-7.
8. Ponnighaus MJ, Fine PEM, Sterne ACJ, Malema SS, Bliss L, Wilson RJ. Extended schooling and good housing conditions are associated with reduced risk of leprosy in rural Malawi. Int J Lepr Other Mycobact Dis. 1999;62(3):345-52.
9. Desikan KV, Sudhakar KS, Tulasidas I, Rao PV. Observations on reactions of leprosy in the field. Ind J Lepr. 2007;79(1):1-8.
10. Sehgal VN, Gautam RK, Koranne RV, Beohar PC. The histopathology of type I (lepra) and type II

(ENL) reactions in leprosy. Ind J Lepr. 1986;58:417-21.
11. Nigam P, Mukheja RED. A study of reactions among 398 patients of leprosy. Indian J Dermatol Venereol Leprosy 1975;41:5.
12. Lockwood PNJ, Vinayakumar S, Stanley JNA. Clinical features and outcome of reversal (type I) reactions in Hyderabad, India. Int J Lepr. 1993;61(1):8-15.
13. Pfaltzgraff RE, Gopalramu. Clinical leprosy. In: Hastings RC. Ed. Leprosy. 2nd ed, Edinburgh London Madrid Melbourne New York and Tokyo: Churchill Livingstone; 1994: 193-224.
14. Jopling WH, Mc Dougall AC. Leprosy reactions (Reactional states). The hand of Leprosy. 5th Edn, CBS publishers and distributors, New Delhi; 1996: 82-91.
15. Van Brakel WH, Khawas IB, Lucas BS. Reactions in leprosy: an epidemiological study of 386 patients in West Nepal. Lepr Rev. 1994;65:190-203.
16. Radia KB, Ridley DS. The histological course of reactions in borderline leprosy and their outcome. Int J Lepr Other Mycobact Dis. 1981;49(4):383-92.
17. Lucas S. Bacterial diseases. In: Lever's histopathology of the skin. 9th ed. Philadelphia, Baltimore, New York, London, Buenos Aires Hong Kong, Lippincott Williams and Wilkins, Sydney and Tokyo; 2005: 551-590.
18. Job CK. Pathology of leprosy. In: Hastings RC. Ed. Leprosy. 2nd ed. Churchill Livingstone, Edinburgh London Madrid Melbourne New York and Tokyo; 1994: 193-224.

Cite this article as: Nataraj P, Haritha K. A clinical, epidemiological and histopathological study of leprosy reactions. Int J Res Dermatol 2018;4:527-33.