

Research article

Leprosy Reactions: Frequency and Risk Factors

Farhana-Quyum^{1*}, Mashfiqul-Hasan², Wahida Khan Chowdhury³ and M A Wahab⁴

¹Department of Dermatology and Venereology, Ashiyan Medical College Hospital, Dhaka, Bangladesh

²Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

³Department of Dermatology and Venereology, Shahabuddin Medical College Hospital, Dhaka, Bangladesh

⁴Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Abstract

Objective: To observe the frequency and risk factors of reactions in different category of leprosy patients.

Methods: In this observational study 722 leprosy patients [77.8% Paucibacillary (PB) and 22.2% Multibacillary (MB)] were included over a period of 2 ½ years. The clinical & epidemiological details of the patient were recorded during diagnosis and subsequent follow up.

Results: 10.5% patients had leprosy reaction; 7.6% type I and 2.9% type II. 7.1% had reaction at diagnosis and 3.4% during or after completion of treatment. 2.3% (13/562) PB patients had reaction all of which were type I, whereas 39.4% (63/160) of MB patients had reaction (26.3% type I and 13.1% type II). Lepromatous end of the spectrum of leprosy had higher frequency of reaction (71.0% in LL and 64.0% in BL in comparison to 6.0%, 5.3% and 23.1% in TT, BT and BB respectively). Males had higher frequency of type I reaction in comparison to females (male female: 11.3% 3.3%, $p < 0.001$) whereas MB patients had significantly higher frequency in comparison to PB patients (MB PB: 26.3% 2.3%, $p < 0.001$); which was also true for type II reaction (male female: 4.6% 0.9%, $p = 0.003$; MB PB: 13.1% 0.0%, $p < 0.001$). Heavy skin infiltration, higher bacillary load and disability were observed in type II reaction.

Conclusion: Male MB patients at the lepromatous end of spectrum of leprosy had higher frequency of reaction. Type II reaction was less frequent than type I reaction, but was associated with higher degree of skin infiltration and disability along with higher bacillary index.

*Corresponding author: Farhana-Quyum, Department of Dermatology and Venereology, Ashiyan Medical College Hospital, Dhaka, Bangladesh, Tel: +880 1816 268745; E-mail: farhana.quyum@gmail.com

Citation: Farhana-Quyum, Mashfiqul-Hasan, Chowdhury WK, Wahab MA (2016) Leprosy Reactions: Frequency and Risk Factors. J Clin Dermatol Ther 3: 022.

Received: June 30, 2016; **Accepted:** August 19, 2016; **Published:** September 02, 2016

Introduction

Leprosy reaction is an immunological event that may occur before, during or after treatment of leprosy with Multidrug Therapy (MDT). In the era of MDT, while the treatment of leprosy has become well structured leprosy reaction remains to be a great concern as it may cause nerve function impairment leading to permanent disability and often requiring long term immunosuppressive therapy.

Of the two types of reaction occurring in leprosy, type I reaction (Reversal Reaction, RR) is a type-IV hypersensitivity reaction where there is partial shift of cell mediated immunity most frequently observed in borderline categories i.e., Borderline Tuberculoid (BT), Borderline (BB) and Borderline Lepromatous (BL) with a frequency of 30% in these patients [1,2] or in Multibacillary (MB) cases [2]. Age is a relevant additional risk factor for RR occurrence and sequelae [3]. It represents the acute immune episodes of TH1 response to *Mycobacterium leprae* antigen that occurs in skin and nerve and is responsible for nerve function impairment. The skin lesions become acutely inflamed and edematous while the nerves become enlarged tender. RR is frequently recurrent and leading cause of nerve damage. It can occur at any time but are frequently occur after starting MDT or during the puerperium [2].

Type II reaction (Erythema Nodosum Leprosum, ENL) has a prevalence of 24% in leprosy patients [upto 50% in Lepromatous (LL) and 9% in Borderline Lepromatous (BL)]. It is a type-III hypersensitivity reaction caused by extra vascular deposition of immune complexes resulting in neutrophil infiltration and complement activation. ENL affects many organs with an acute onset but can evolve into chronic phase and can be recurrent [4]. Systemic symptoms are more prominent in ENL. It produces fever and painful tender red papules or nodules which occur in crops often affecting the face and extensor surfaces of the limbs. Bullous ENL lesions may ulcerate. Subcutaneous tissue involvement may lead to tethering & fixation to joints causing loss of function. ENL reaction may also produce uveitis, neuritis, arthritis, datylitis, lymphadenitis and orchitis. The prolong inflammation of organs can lead to blindness and sterility. A great infiltration of the skin and a higher bacterial index are two relevant risks for developing ENL [2].

In order to improve strategies for management of reactions, its epidemiology need to be well studied. Very few data regarding the burden of leprosy reactions in our patients is currently available. So the aim of the study was to observe the frequency and risk factors of reactions in different category of leprosy patients as well as to evaluate the characteristics of those with reaction.

Subjects and Methods

In this observational study done, 722 leprosy patients [77.8% Paucibacillary (PB) and 22.2% Multibacillary (MB)] were included over a period of 2 ½ years from January 2011 to June 2013 in six clinics of The Leprosy Mission International Bangladesh (TLMI-B) Dhaka Program. The clinical & epidemiological details of the patient were recorded during diagnosis and subsequent follow up (varying

from 6 months to 2 ½ years). Diagnosis was based on clinical ground by the cardinal signs of leprosy and supported by Bacillary Index (BI) in slit skin smear. Type I reaction was diagnosed when the lesions were raised, warm and erythematous with enlarged, tender peripheral nerve adjacent to the lesion, whereas type II reaction was diagnosed by the presence of multiple tender nodules with systemic features [1]. Disability grading was recorded as suggested by World Health Organization (WHO) [5]. Written informed consent was taken from the participants. The study was approved by TLMi-B.

Result

The detail epidemiological indicators of the study population were published previously [6]. Among 722 leprosy cases 10.5% patients had leprosy reaction of which frequency of type I reaction was higher than type II (7.6% 2.9%). 7.1% had reaction at diagnosis and 3.4% during or after completion of treatment. Only 2.3% (13/562) patients with PB leprosy had reaction all of which were type I. On the other hand 39.4% (63/160) of MB patients had reaction (26.3% type I and 13.1% type II) (Table-1). Type II reaction exclusively included LL and BL patients (19/21 and 2/21) while type I reaction was mostly confined to borderline cases (48/55) but also involved a few cases of TT and LL (7/55). Lepromatous end of the spectrum of leprosy had higher frequency of reaction (71.0% in LL and 64.0% in BL in comparison to 6.0%, 5.3% and 23.1% in TT, BT and BB patients respectively) (Table-2).

Type of reaction	No. of Cases	PB	MB
N	722	562	160
Type I reaction	55 (7.6)	13 (2.3)	42 (26.3)
Type II reaction	21 (2.9)	0 (0.0)	21 (13.1)
Combined	76 (10.5)	13 (2.3)	63 (39.4)

Table 1: Frequency of type I and II reaction.

Within parenthesis are percentages over column total.

Ridley-Jopling class	Type I	Type II	No reaction	Total
TT	4 (6.0)	0 (0.0)	63 (94.0)	67
BT	31 (5.3)	0 (0.0)	554 (94.7)	585
BB	3 (23.1)	0 (0.0)	10 (66.9)	13
BL	14 (56.0)	2 (8.0)	9 (36.0)	25
LL	3 (9.7)	19 (61.3)	9 (29.0)	31
PN	0 (0.0)	0 (0.0)	1 (100.0)	1
Total	55 (7.6)	21 (2.9)	646 (89.5)	722

Table 2: Frequency of type I and II reaction in different forms of leprosy according to Ridley-Jopling classification.

Within parenthesis are percentages over row total.

It was observed that males had significantly higher frequency of RR in comparison to females (male vs female: 11.3% 3.3%, $p < 0.001$) whereas MB patients had significantly higher frequency of RR in comparison to PB patients (MB PB: 26.3% 2.3%, $p < 0.001$) which was also true for ENL (male vs female: 4.6% vs 0.9%, $p = 0.003$; MB PB: 13.1% 0.0%, $p < 0.001$) (Table-3).

As shown in table-4 frequency of heavy skin infiltration was significantly higher in patients with type II reaction, whereas mild infiltration was higher in those with type I reaction. Most of the patients with type I (60.0%) and type II (81.0%) reaction had involvement of >2 nerves. Presence of disability was higher in patients with type II reaction (type I 36.4% type II 61.9%; $p = 0.069$). Higher

bacillary load was also observed in patients with type II reaction (BI ≥ 3 : type I 37.1% vs type II 90.5%).

Risk factor	No. of Cases (N=722)	Cases with RR (n=55)	Cases with ENL (n=21)
Spectrum			
PB	562	13 (2.3)	0 (0.0)
MB	160	42 (26.3)	21 (13.1)
p-value*	-	<0.001	<0.001
Gender			
Male	390	44 (11.3)	18 (4.6)
Female	332	11 (3.3)	3 (0.9)
p-value*	-	<0.001	0.003

Table-3: Risk factors for reactions. *by χ^2 test.

Within parenthesis are percentages over row total.

Attribute	Type I (n=55)	Type II (n=21)	p value
Skin infiltration			
Mild	31 (56.4)	04 (19.0)	
Moderate	13 (23.6)	06 (28.6)	0.006
Heavy	11 (20.0)	11 (52.4)	
Nerve involvement			
None	07 (12.7)	02 (9.5)	0.193
1-2	15 (27.3)	02 (9.5)	
>2	33 (60.0)	17 (81.0)	
Disability			
Absent	35 (63.6)	08 (38.1)	0.069
Present	20 (36.4)	13 (61.9)	
Bacillary index**			
<3	22 (62.9)	2 (9.5)	<0.001
≥ 3	13 (37.1)	19 (90.5)	

Table-4: Frequency of different parameters in type I and II reaction.

*by χ^2 test; **not done in 20 patients with type I reaction.

Within parenthesis are percentages over column total.

Discussion

In the present study carried out over two and half years in urban leprosy clinics of Dhaka leprosy reaction was diagnosed in 10.5% of leprosy cases. Frequency of reaction was higher in male, MB leprosy and those in the lepromatous end of spectrum of leprosy. As expected type II reaction was diagnosed only in LL and few BL cases and type I reaction was mostly present in borderline cases. Overall type I reaction was more frequent than type II, but frequency of heavy skin infiltration and disability were higher in type II.

Frequency of reaction was observed to be higher in other studies than that observed in present one [7-11] which may be due to variability in follow up period. Our study found that, around 2/3 of patients having reaction was identified at diagnosis of leprosy; rest 1/3 developed features of reaction during or even after successful treatment of leprosy. It may reflect the tendency of our people to seek medical attention only when they develop symptoms of reactions despite harboring leprosy for several months or even years before. However it is also vital to monitor every patient for development of signs of reaction during and after treatment as unidentified reaction may add to the disability brought by the disease itself.

The risk of developing reaction is not same in all leprosy patients. We found that in MB cases especially in those with lepromatous

leprosy frequency of reaction was higher. Similar result was found in other studies [9-13]. So these groups of patients are in need of strong surveillance for development of reaction. Male patients had higher frequency of reaction in the present study which is different to observation of other studies [9]. This may reflect the health seeking behavior of our population where female are often reluctant to seek medical attention due to social stigma.

When comparing two types of reaction disability was found to be more frequent in those with type II reactions. It may reflect the disease burden as type II reaction occurred in patients with comparatively high bacillary load and heavy skin infiltration in addition to effects of reaction.

Conclusion

Reactions are not infrequent in leprosy. Patients who were male had MB leprosy and those at the lepromatous end of spectrum of leprosy had higher frequency of reaction. Type II reaction was less frequent than type I reaction, but was associated with higher degree of skin infiltration and disability along with higher bacillary index.

Acknowledgement

We thank all the staff of TLMI-B Dhaka program for their hard work in case detection and data collection. We are also grateful to the TLMI-B authority to give us permission to carry out the study and Dr. C. Ruth Butlin (DBLM Hospital, Nilphamari, Bangladesh) for her kind co-operation.

References

1. James WD, Berger TG, Elston DM (2011) *Andrew's diseases of the skin: Clinical Dermatology* (11th edn.). Saunders Elsevier, Philadelphia, USA, Pg no: 334-44.
2. Walker SL, Lockwood DN (2006) The clinical and immunological features of leprosy. *Br Med Bull* 77-78: 103-121.
3. Ranque B, Nguyen VT, Vu HT, Nguyen TH, Nguyen NB, et al. (2007) Age is an important risk factor for onset and sequelae of reversal reactions in Vietnamese patients with leprosy. *Clin Infect Dis* 44: 33-40.
4. Pocaterra L, Jain S, Reddy R, Muzaffarullah S, Torres O, et al. (2006) Clinical course of erythema nodosum leprosum: an 11-year cohort study in Hyderabad, India. *Am J Trop Med Hyg* 74: 868-879.
5. Ministry of Health and Family Welfare (2005) National guidelines and technical manual on leprosy (3rd edn.). Government of Bangladesh and World Health Organization, Pg no: 4-55.
6. Farhana-Quyum, Mashfiqul-Hasan, Chowdhury WK, Wahab MA (2015) Epidemiological indicators and clinical profile of leprosy cases in Dhaka. *Journal of Pakistan Association of Dermatologists* 25:191-196.
7. Lockwood DN, Vinayakumar S, Stanley JN, McAdam KP, Colston MJ (1993) Clinical features and outcome of reversal (type 1) reactions in Hyderabad, India. *Int J Lepr Other Mycobact Dis* 61:8-15.
8. Roche PW, Master JL, Butlin CR (1997) Risk factors for type 1 Reactions in leprosy. *Int J Lepr Other Mycobact Dis* 65:450-455.
9. Kumar B, Dogra S, Kaur I (2004) Epidemiological characteristics of leprosy reactions: 15 years experience from North India. *Int J Lepr other Mycobact Dis* 71: 125-133.
10. Becx-Bleumink M, Berhe D (1992) Occurrence of reactions, their diagnosis and management in leprosy patients treated with multidrug therapy; experience in the leprosy control program of the All Africa Leprosy and Rehabilitation Training Center (ALERT) in Ethiopia. *Int J Lepr Other Mycobact Dis* 60:173-184.
11. Jacob JT, Kozarsky P, Dismukes R, Bynae V, Margoles L, et al. (2008) Short report: five-year experience with type 1 and type 2 reactions in Hansen disease at a US travel clinic. *Am J Trop Med Hyg* 73:452-54.
12. Khan MZ, Saeed S (2005) Reactions in Leprosy. *JPMI* 19: 334-338.
13. Teixeira MA, Silveira VM, Franca ER (2010) Characteristics of leprosy reactions in paucibacillary and multibacillary individuals attended at two reference centers in Recife, Pernambuco. *Rev Soc Bras Med Trop* 43: 287-292.