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Original Research Article

The scenario of lepra reactions in a tertiary care hospital in central Karnataka

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ABSTRACT

Background: Leprosy is a chronic disease with a benign course. Even though it is a curable disease, due to presence of bacilli in tissue hypersensitivity reaction may develop called lepra reactions. This study is conducted to see the number of patients with reactions, their onset, presentation, course and response to treatment.
Methods: This is a retrospective study conducted over the period of 2 years from January 2017 to December 2019 in a tertiary care hospital of JJM Medical College at Davanagere. All confirmed cases after doing biopsy were included in the study. All the cases were classified according to Ridley-Jopling classification. Treatment was started based on World Health Organization (WHO) criteria for paucibacillary and multibacillary, for the duration of 6 months and 12 months accordingly.
Results: Over the period of 2 years 178 cases of leprosy were registered. The majority of patients were seen in borderline tuberculoid leprosy spectrum (BT) that is in 29.2% of the patients, followed by in lepromatous leprosy (LL) seen in 26.4% of the patients. Lepra reactions were seen in 41 (23.03%) patients. Type 2 reaction (T2R) were more commonly observed that is in 27 patients (65.8%), type 1 reaction (T1R) is seen in 14 patients (34.1%). T2R were observed more commonly in LL spectrum.
Conclusions: Reactions are more damaging than the disease itself. Hence, early diagnosis and proper management is important to prevent further reactions. This is can be done by good clinical knowledge about the disease and reactions and proper follow up of cases.

Keywords: Leprosy, Lepra reactions, Prevalence

INTRODUCTION

The causative agent of leprosy, mycobacterium leprae which was identified by Armauer Hansen in 187.[1] Leprosy has predilection for skin and peripheral nerves as lepra bacilli grows best in cooler areas.[2] After introduction of multidrug therapy by World Health Organization (WHO), the duration of therapy has been shortened. Lepra bacilli will be present in deeper tissues even after varying period of chemotherapy, residual bacteria and/or bacterial fragments must be cleared by immune system, hence patients may be still prone for reactions even though declared cured.[3] A reaction in leprosy is usually defined as an acute episode occurring in the otherwise chronic course of the infection, and which appears to have an allergic basis.[4] Lepra reactions usually cause symptoms which compels patient to visit doctor. Leprosy has been successfully eliminated from India, with a current prevalence rate of 0.66 in 1000 of population and an annual new case detection rate of 9.71 in 1,00,000 population.[5]

Leprosy is a curable disease, but due to presence of bacilli in tissue and because of hypersensitivity reaction of the body lepra reaction do occur. We have noticed many cases of lepra reactions in central part of Karnataka. Hence this retrospective study is conducted to see the number of patients with reactions, their onset, presentation, course and response to treatment.

METHODS

A retrospective data analysis of all the leprosy cases registered at the department of dermatology, venerology and leprosy in a tertiary care hospital, JJM Medical College, Davanagere, Karnataka, India after taking approval from the ethical committee approval. The study period lasted from January 2017 to December 2019.

The confirmed cases of leprosy after doing biopsy were included. 178 patients were diagnosed with Hansen's over the period of 2 years among which 41 (23.03%). Other investigations which were done includes split skin smear, complete blood count (CBC), renal function test (RFT), liver function test (LFT), X-ray, random blood sugar (RBS), Glycated hemoglobin (HbA_1c) to rule out diabetic in cases of trophic ulcer. All the cases had been taken detailed medical history and examined thoroughly by doing complete examination including general physical examination, vitals, cutaneous examination, nerve examination, eye, joints, mucosa and other systemic examination. The diagnosis of leprosy was based on the Ridley-Jopling classification, which is based on a detailed morphological, bacteriological, immunological and histopathological examination. Also, cases were classified according to WHO criteria as multibacillary (MB) and paucibacillary if skin lesions were more than 6 or positive bacteriological index (BI) and if skin lesions were less than 5 and negative BI respectively.

Following biopsy report patient were started on multidrug therapy for paucibacillary and multibacillary for 6 months and 12 months respectively according. Patients were also advised to report immediately to the hospital if they develop any symptoms like fever, arthalgia, myalgia, redness and swelling of cutaneous lesions, acute tenderness of nerves, edema of hands and feet. All the diagnosed cases of Hansen's disease were evaluated for the type of reaction, onset, clinical presentation, frequency of occurrence, triggering factors, course of disease, deformities and management of reactions.

All the patients with mild reactions were treated with rest and paracetamol, while those with severe reactions were treated with 40mg of prednisolone, followed by 30 mg, 20 mg, 15 mg, 10 mg, and 5 mg each over the period of 2 weeks. If patient is still on MDT, MDT is continued. In recurrent ENL that is patients who developed reactions after 3 months of control of reaction along with prednisolone, clofazamine 100 mg TDS for 1 month, followed by BD and OD for 1 month each. For chronic reactions, that is patient who developed reaction within 3 months of control of reaction thalidomide and clofazimine were started along with prednisolone.

Statistical analysis

The date was entered in Microsoft excel and statistical package for the social sciences (SPSS) version 25 was used for statistical analysis. Qualitative data was expressed in the form of frequency, percentage and graphs.

RESULTS

Over a period of 2 years, 178 patients were diagnosed with Hansen's disease (Table 1). Males outnumbered females, males were 109 and females 69. The majority of patients were seen in borderline tuberculoid leprosy spectrum (BT) that is in 29.2% of the patients, followed by in lepromatous leprosy (LL) that is in 26.4% of the patients. Lepra reactions were seen in 41 patients. Type 2 reaction (T2R) were more commonly observed in 27 patients (65.8%), type 1 reaction (T1R) is seen in 14 patients (34.1%). T2R were observed more commonly in lepromatous leprosy (LL) spectrum. T1R were more commonly seen in borderline tuberculoid spectrum (BT) spectrum (Table 2). Among the age distribution, most common age group for T2R is 31-45 years, which includes 13 patients (48.1%), next common is 46-60 years which included 9 patients (33.3%). The most common age group for T1R is 46-60 years which consist of 8 patients (57.1%) followed by 31-45 years which included 5 patients (35.7%) (Table 3). Triggering factor couldn't be found out in any patient. Deformities like trophic ulcer is present in 3 patients and no patient developed deformity after completion of treatment. Co-morbidities like diabetes mellitus were seen in 10 patients and 6 patients had hypertension.

Most of the Patients of T1R presented with redness and swelling of cutaneous lesions and acute nerve tenderness. 3 (21.4%) out of patients 14 patients had mild symptoms, remaining 11 (78.5%) patients had severe symptoms. 2 patients had edema of feet. All the patients that are 27 patients of T2R had tender erythematous nodules, 8 (29.6%) patients just had tender erythematous nodules without any other symptoms. 14 (51.85%) patients presented with fever along with it, 16 (59.2%) patients had nerve tenderness along with skin lesions, 6 (22.2%) patients had complained joint pain, 2 (7.4%) patients had blister along with other skin lesions, 2 (7.4%) patients had epididymo-orchitis. Among patients with T1R with mild symptoms 2 patients had bacillary index (BI) of 2+, 1 patient had bacillary of 3+, whereas patients with severe symptoms showed 1 patient with bacillary index of 1+, 5 patients with bacillary index of 2+ and 4 patients with bacillary index of 3+. Statistical analysis showed p value of 0.858 which showed statistically insignificant association. Among patients of T2R with mild symptoms 2 patients had BI of 3+, 2 patients had bacillary of 4+, 6 patients had BI of 5+ and 2 patients showed BI of 6+ whereas patients with severe symptoms showed 2 patients with bacillary index of 4+, 8 patients with bacillary index

of 5+ and 5 patients showed BI of 6+. Statistical analysis showed p value of 0.512 which tells that association is not statistically significant (Table 6).

Following treatment with single course of tapering steroids according to WHO protocol, 9 out 11 patients who had severe T1R and 13 out of 16 patients who had severe T2R were relieved of symptoms, all the patients' showed response to steroids. Recurrent reactions were seen in 14 (34.1%) out of total 41 cases of lepra reactions. 5 (12.1%) out of 41 patients had chronic T2R. Patients who had subsequent episode of ENL occurring within 28 days or more stopping treatment and patients who had developed ENL within 27 days of stopping treatment were labelled as recurrent ENL and chronic ENL. The patients of recurrent or chronic ENL were started on clofazimine and prednisolone.

Clofazamine was given at the dose of 100 mg thrice daily for 2-3 months, later tapered to 100 mg twice daily for 3 months and 100 mg daily as long as symptoms persisted along with prednisolone, which was started at the dose of 30 mg daily for 2 weeks which is later tapered to 20 mg, 15 mg, 10 mg, then 5 mg for 2 weeks. 5 patients recurred with reaction within 27 days of completion of treatment and 2 patients presented after a month of completion of treatment who were started on thalidomide and prednisolone. Thalidomide was given in the dose of 200 mg twice daily for a week, the tapered 100 mg morning and 200 mg in the evening for 4 weeks, then 200 mg in the evening, 100 mg in the evening each for 4 weeks and later 100 mg in the evening alternate day for 8 weeks along with prednisolone as above, all the patients were responsive to the regimen.

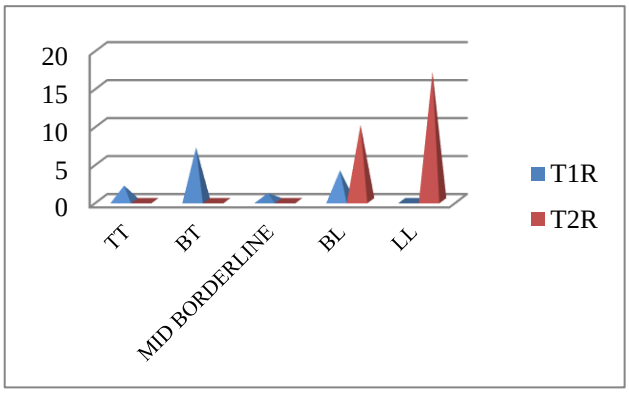

Figure 1: Prevalence of lepra reactions.

Table 1: Distribution of leprosy patients.

Type of leprosy	Male	Female	Total	Percentage (%)	P value
Tuberculoid tuberculoid (TT)	17	5	22	12.3	0.38
Borderline tuberculoid (BT)	26	21	47	26.4	
Mid borderline	1	-	1	0.5	
Borderline lepromatous (BL)	21	18	39	21.9	
Lepromatous leprosy (LL)	31	21	52	29.2	
Pure neuritic	4	1	5	2.8	
Histoid	9	3	12	6.7	
Total	109	69	178		

Table 2: Prevalence of reactions.

Type of leprosy	T1R	Percentage (%)	T2R	Percentage (%)	P value
TT	2	14.2	-	-	0.0001
BT	7	50	-	-	
Mid borderline	1	7.1	-	-	
BL	4	28.5	10	37.03	
LL	-	-	17	62.9	
Total	14		27		

Table 3: Occurrence of T1R with respect to treatment.

Type of leprosy	Before initiation of treatment	After initiation of treatment	After completion of treatment	Total
TT	1	1	-	2
BT	1	5	1	7
Mid borderline	-	1	-	1
BL	-	3	1	4
LL	-	-	-	-
				14

Table 4: Occurrence of T2R with respect to treatment.

Type of leprosy	Before initiation of treatment	After initiation of treatment	After completion of treatment	Total
TT	-	-	-	
BT	-	-	-	
Mid borderline	-	-	-	
BL	1	7	2	10
LL	1	13	3	17
				27

Table 5: Age distribution of reactions.

Age distribution (in years)	T1R	T1R	Total	T2R	T2R	Total	P value
	Male	Female		Male	Female		
0-14	-	-	-	1	-	1	0.19
15-30	1	-	1	4	-	4	
31-45	4	1	5	11	2	13	
46-60	6	2	8	7	2	9	
>60	1	-	1	1	-	1	
Total	11	3	14	23	4	27	

Table 6: Distribution of patients according to severity and bacillary index.

Type of reaction	Severity	Number of patients	Bacillary index						P value
			1+	2+	3+	4+	5+	6+	
T1R	Mild	3	-	2	1	-	-	-	0.858
	Severe	11	2	5	4	-	-	-	
T2R	Mild	12	-	-	2	2	6	2	0.512
	Severe	15	-	-	-	2	8	5	

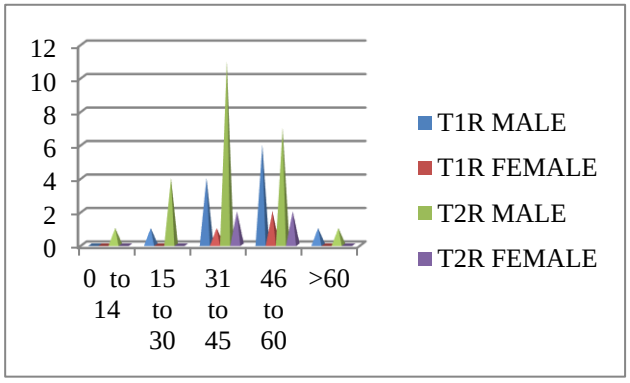

Figure 2: Age distributions of reactions.

DISCUSSION

Leprosy is a disease which is known for its low infectivity and chronic course.[2] Leprosy is often complicated by lepra reactions through hypersensitivity reactions which leads to greater inflammation and damage. Lepra reactions can be a presenting manifestation uncommonly, it can occur even before initiation of treatment with multidrug therapy, or after completion of treatment.[6] If reactions occur before initiation of treatment, when fever is the predominant complaint with other systemic manifestations without any obvious skin of leprosy or there is no past history of leprosy, diagnosis will be quite challenging.[6]

The movement towards lepromatous leprosy is associated with a clinical and histological disturbance which makes up "downgrading reaction", whereas the movement towards tuberculoid leprosy is associated with the features of "reversal reaction".[4] T1R is a type IV hypersensitivity reaction, involves Th1 cell response by increasing levels of TNF-a, IFN-g, IL-2 and IL-4 cytokines. Alternatively, this reaction may also be a downgrading reaction, or a reversal reaction, commonly occurs in patients with borderline or tuberculoid forms of leprosy.[7] T1R often characterized by inflamed plaque, usually tender, with or without edema of hands and feet and neuritis and lasting for months to years.[8]

Type 2 lepra reaction, also known as erythema nodosum leprosum (ENL), is an immune complex mediated hypersensitivity reaction. T2R occur in patients with polar lepromatous or borderline lepromatous leprosy.[6] Type 2 lepra reaction can be associated with fever, systemic manifestations like polyarthritis, lymphadenopathy, immune complex glomerulonephritis, epididymoorchitis

and iridocyclitis.[9] NLEP guidelines on lepra reactions have differentiated clearly between mild and severe T1R, T2R, as well as basic differences between the two types of reaction.[10] Risk factors for T2R includes LL with skin infiltration, bacteriologic index >4, anti-leprosy drugs expect clofazamine, trauma, surgical intervention, intercurrent infection, stress, immunization, parturition, pregnancy, and drugs like potassium iodide.[2]

Implementation of MDT has decreased the incidence of reactions. In a study conducted by Kumaran et al observed that a fourfold reduction in the incidence of late lepra reactions in patients who received MDT compared to patients only undergoing dapsone monotherapy.[11]

In our study, 29.2% of patients had borderline tuberculoid leprosy, followed by lepromatous leprosy in 26.4% of the patients which is contrast to study conducted by Verma et al.[2] In other studies conducted in neighbouring countries BT Hansens is the most common.[12-14] Most of the cases of Hansen's belonged to middle age group which similar to study conducted by Chhabra et al and Jindal et al.[13,15]

We found 23.03% of patients with lepra reactions in our study which is less compared to Verma et al where they showed 62.1% with lepra reactions. Among 178 patients T1R is seen in 34.1% of the patients which is less comparable to study conducted by Chhabra et al where they showed 30.4% of patients presented with T1R, and Kumar et al 30.9%.[16] Among the 14 patients who had T1R only 2 (14.2%) patients had reaction at the time of diagnosis. Who presented with inflamed erythematous plaques along with nerve tenderness which is contrast in Verma et al where they have seen maximum level of patients presented to them with a reaction (65.8%) at the time of the diagnosis of Hansen's disease. T2R is seen in 65.8% of the patients in our study. Among these only 2 (7.4%) patients among 27 patients had reactions at the time of diagnosis and these patients presented with tender erythematous nodules, high grade fever and arthalgia. Where as in a study conducted by Manandhar et al, they observed 34% of the patients had T2R at the time of presentation, 32% developed it within 6 months and 19%- after one year of treatment.[17]

In our study, T1R was seen maximum in BT>BL>TT>mid-borderline (50%>28.5%>14.2%>7.1%). Compared to Verma et al T1R was seen in the maximum BL>BT>TT (10.60%, 6.06%, 1.51% respectively.[2] Sharma et al showed the maximum prevalence of T1R in BB>BL>BT>LL (23.3%, 18.18%, 6.25%, 3.25% respectively.[12] Chhabra et al showed T1R is common in BT Hansens's (65.9%) similar to our study, which is also consistent in many other studies.[18,19] Triggering factor was found in any patient, compared to 80-84% of patients with no triggering factors in T1R and T2R in a study by Prasannan et al.[20]

Lepra reactions are managed mainly with corticosteroids, thalidomide, clofazamine and other steroid sparing agents like methotrexate, cyclosporine, azathioprine, mycophenolate mofetil.[21] Corticosteroids like prednisolone is effective in acute reactions, clofazamine is added in chronic and recurrent reactions as long-term use of prednisolone lead to steroid induced side effects and recurrence after withdrawal of medication. Proper and timely management of lepra reactions is necessary to prevent progression of sensorimotor deficit and subsequent development of deformity. In a study conducted in our institute from the period 2015 to 2018 by Mangala et al, trophic ulcers were seen in 37.16%, 33.62% of resorption of fingers and toes, 32.74% of claw hand, 10.6% of foot drop.[22] Hence early diagnosis and adequate treatment is important. While examining a case of leprosy, it is important to do complete examination of skin lesions, and peripheral nerve examination for prevention of further deformities. After examination, educate the patient about self-care, daily inspection of hands and feet.

Limitations

As it is retrospective study follow up has not been possible and hence true incidence of late reactions has not been found out. Secondly, as many patients were from poor economic background thalidomide could not be used in many patients.

CONCLUSION

We conclude that even though leprosy is a benign and chronic disease, reactions are commonly encountered. Reactions are more damaging than the disease itself. Hence early diagnosis and proper management is important to prevent further reactions. This is can be done by good clinical knowledge about the disease and reactions and proper follow up of cases.

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