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Original Article

Clinico-epidemiological Profile of Erythema Nodosum Leprosum Cases in Western Odisha

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This study was carried out in a hospital setting in Odisha to find out the epidemiological profile and clinical spectrum of ENL and their association with bacillary load, clinical types of leprosy and comorbid conditions of leprosy patients. Out of 1352 cases of leprosy, 97 were diagnosed with ENL. Male patients outnumbered the females (4.3:1), and leprosy patients in their 3rd and 4th decade were more commonly found to be having ENL. Majority of the patients belonged to the lepromatous leprosy (LL) spectrum (74.22%). A positive family history of Leprosy was obtained in 7.21% of cases. Diabetes mellitus followed by hypertension was the most common comorbid condition. Whether these conditions have any direct link with ENL needs to be investigated by proper prospective studies. 79.38% of cases had arthritis whereas glomerulonephritis and peripheral edema were observed in 29.89% of cases each. Observations of this study will be useful for planning field based studies in population from Odisha.

Key words: ENL, Epidemiological Profile, Clinical Profile, Odisha, India

Introduction

Leprosy, an ancient disease, affects the skin, peripheral nerves and other organs, is caused by *Mycobacterium leprae*, an obligate intracellular parasite. It's a kind of unique disease with two poles in its clinical spectrum. In the tuberculoid pole, where the cell mediated immunity (CMI) is high, the disease tends to have fewer but sharply defined lesions and involvement of nerve trunks. On the other hand, patients in the lepromatous pole present with a low CMI, high bacillary load and multiple ill-defined skin lesions (Boggild et al

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2004). The incidence of leprosy has significantly decreased worldwide after the introduction of Multi drug therapy, however, it is still remain an important public health problem in few countries like India, Brazil and Myanmar.

Reactions in leprosy are immunologically mediated episodes of acute inflammation that interrupt the otherwise slow course of leprosy. Reactions are important because they are the major cause of nerve function impairment as well as involvement of organ systems which lead to leprosy associated disability.

Erythema nodosum leprosum (ENL) or Type-2 lepra reaction is a manifestation of type-III hypersensitivity response or Arthus phenomenon. It can present in acute, recurrent or chronic forms. Its incidence among leprosy cases varies from about 10% in borderline cases to as high as 50% among lepromatous leprosy patients (Negera et al 2017). Overall incidence of ENL among MB cases was found to be 8.9% in one Indian cohort (Desikan et al 2007). It can appear before, during or after completion of MDT therapy. Multiple episodes and chronicity are observed more commonly in ENL than Type-1 lepra reaction and probably this is the reason why ENL patients seek hospitalization (Levy et al 1973).

Leprosy is usually associated with poverty and as the economically productive age group is affected more commonly, there is an associated financial implication to it. The western part of Odisha used to be an endemic region for leprosy for a long time and in some of the districts, the prevalence is high even in the post-elimination era. In certain areas, majority of patients may be have agricultural and low income background and belong to rural areas; where the job related migration and lower access rate to available treatment facilities predispose them more to leprosy and therefore ENL.

The aim of the study was to evaluate demographic details and clinical profile of ENL and also to study the association between ENL and clinical spectrum of leprosy, bacillary load and other systemic and cutaneous co-morbid conditions. There is a paucity of systematic studies on the epidemiology of ENL in Odisha. Data generated from this study, particularly the correlation of ENL with bacillary index and systemic co-morbidities could be helpful in formulating strategies to lower the incidence and severity of ENL in the population from where these patients are coming.

Patients and Methods

It was a hospital based prospective study was carried out between September 2015 and September 2017 where all patients diagnosed with leprosy attending the OPD and some also admitted in indoor wards of VIMSAR, Burla presenting with Erythema Nodosum Leprosum were included in the study.

A patient was clinically diagnosed as ENL and included in the study when he/she presented with erythematous, tender nodules or plaques that were evanescent and appearing in crops.

A detailed history in all patients regarding demographic details such as age, sex, socio-economic status (Kuppuswamy 1981), literacy status, area of residence and clinical details such as number of episodes of ENL, past history of treatment for Hansen's disease, ENL or any other co morbidities, family history of leprosy and presence of any history of significant health problems other than Hansen's disease were taken.

All cases enrolled into the study underwent detailed clinical examination. Proper clinical examination was done to determine status of Hansen's disease, nerve involvement. Diagnosis of Erythema Nodosum Leprosum was made clinically (Negera et al 2017). Investigations like

slit skin smear for Acid Fast Bacilli (AFB) and biopsy for histopathological diagnosis of leprosy were done in all cases.

Results

During the study period 1352 cases of leprosy patients had reported out of which 168 (12.42%) were in reaction. 71 (5.25%) patients had Type 1 reaction and 97 patients (7.17%) were clinically diagnosed to be having ENL and were enrolled into the study.

The majority of patients were male 79 (81.4%), with male female ratio of 4.38:1 (79/18). Most of the patients were in the age group of 21-40 years (70.09%). Mean and median age of ENL patients was found to be 34.7±11.31 years and 35 years respectively (Table 1). Out of 97 patients, 84 (86.59%) patients were from rural area and 13 (13.4%) patients from urban area. Majority of patients 55 (56.7%) belonged to lower socio-economic status. Majority of patients 32 (32.98%)

Table 1 : Demographic details of ENL patients included in the study

Characteristic	Number	Percentage
Gender		
Male	79	81.4
Female	18	18.6
Age Distribution (in years)		
0-10	0	0
11-20	6	6.18
21-30	37	38.14
31-40	31	31.95
41-50	16	16.49
51-60	05	5.15
>61	2	2.06
Residence		
Rural	84	86.59
Urban	13	13.40
Socioeconomic status		
Upper	01	1.03
Upper-middle	05	5.15
Lower-middle	14	14.43
Upper-lower	22	22.68
Lower	55	56.70
Educational status		
Illiterate	32	32.98
Primary	27	27.83
Secondary	29	29.89
Graduate and above	09	9.27

Table 2 : Number of ENL episodes experienced by patients

Number of ENL episodes	At Presentation	During follow up
Single	35 (36.08%)	26 (26.8%)
Second	16 (16.49%)	30 (30.92%)
Third	7 (7.21%)	9 (9.27%)
Fourth	5 (5.15%)	2(2.06%)
More than 4	34 (35.05%)	30 (30.92%)

Table 3 : Onset of ENL in relation to MDT

MDT Status	No of Cases
Not started	25(25.77%)
On MDT	34(35.05%)
Completed MDT (< 1 year)	20(20.6%)
Completed MDT (1-2 years)	9(9.2%)
Completed MDT (>2 years)	9(9.2%)

Table 4 : Bacillary Index (BI) of ENL patients

Sl No	BI	No of Cases
1	0	07 (7.21%)
2	1+	12 (12.37%)
3	2+	15 (15.46%)
4	3+	13 (13.40%)
5	4+	50 (51.54%)

Table 5 : Co-morbidities associated with ENL

Sl No	Co-Morbidities	No of cases
1	Hypertension	7 (7.21%)
2	Diabetes Mellitus	11 (11.34%)
3	Chronic Obstructive Pulmonary Disease	4 (4.12%)
4	Chronic Kidney Disease	1 (1.03%)

were found to be illiterate followed by the group of 29 (29.89%) patients had up to secondary level education.

Out of total 97 patients, 7 (7.21%) patients had family contact history of leprosy.

When the clinical subtypes of leprosy was considered, it was found that 72 patients (74.22%) belonged to LL category, making it the most common subtype. BL, BT and BB were seen in 13 (13.4%), 11 (11.34%) and 1 (1.03%) cases respectively.

Classical ENL i.e. the nodular form was the most common morphological variant seen in 84 (86.59%) patients, wheras 19 (19.58%) patients had necrotic lesions and bullous pattern was observed in 13 (13.4%) patients.

When enquired about the number of episodes, 36.08% of cases revealed that they sought health care at the onset of the first episode itself but an almost equal number of patients came to the hospital for the first time only after the 4th episode. During follow up, maximum patients had either two (30.92%) or even more than 4 episodes (Table 2).

In 25.77% of the cases, ENL appeared for the first time even before MDT was started (Table 3). However, 35.05% had ENL when they were continuing MDT and it appeared for the first time after the completion of MDT in 39% of the patients. Out of those who had completed MDT, ENL appeared for the first time within less than 1 year of stoppage of the drug in majority (20.6%) of the cases.

Among all cases of ENL enrolled into the study, a high Bacillary Index of 4+ was observed to be associated with highest incidence of ENL (Table 4).

Table 6 : Systemic involvement observed in ENL patients

Sl No	Systemic Association	No of Cases
1	Arthritis	77 (79.38%)
2	Peripheral Edema	29 (29.89%)
3	Glomerulonephritis	29 (29.89%)
4	Lymphadenitis	7 (7.21%)
5	Ocular Changes	8 (8.24%)
6	Raised liver enzymes	9 (9.27%)
7	Orchitis	5 (5.15%)

Table 7 : Nerve involvement in ENL cases

Number of Nerves Involved	No of Cases
1	14 (14.43%)
2	32 (32.98%)
3	16 (16.49%)
4	06 (6.18%)
Clinical manifestation	
Nerve enlargement	68 (70.10%)
Tenderness	49 (50.51%)
Hypoaesthesia/Anesthesia	52 (53.60%)
Motor weakness	13 (13.40%)
Palsy	8 (8.24%)

About 24% of all ENL patients had some significant comorbidities. Diabetes mellitus (11.34%) followed by hypertension (7.21%) were the most commonly observed comorbidities (Table 5).

When the incidence of systemic association was studied, arthritis was the most common systemic association found in 79.38% of the cases (Table 6). Peripheral edema and glomerulonephritis were seen in 29.89% of ENL cases each.

Around 70% of the cases had nerve involvement. 32.98% patients had involvement of two nerves whereas involvement of 3 and 4 nerves were observed in 16.49% and 6.18% of the cases respectively (Table 7). Nerve enlargement was the most common manifestation seen in 70.10% of ENL patients followed by hypoaesthesia or anesthesia and tenderness.

Discussion

In almost all studies conducted on ENL, a definite male preponderance has been observed. Males outnumbered female in studies conducted by Motta et al (2012) reported 68% male patients, Walker et al (2014) found 73.68% male cases, Guerra et al (2004) reported 60% male cases, Dutta (1979) reported 84% male and Prasad et al (2013) reported 68.18% male cases. In current study, out of 97 cases, 81.4% cases were male and 18.6% cases were female. One of the possible causes of this could be because of social factors and gender specific health seeking behavior of the patients.

In current study mean and median age were calculated to be 34.70 ± 11.31 years and 35 years respectively, and most of the cases belonged to the 21 to 40 years age group (68 patients). This finding is consistent with the various studies such as that of Pocaterra et al (2006) reported mean age 34.7 years, Walker et al (2015) (ENLIST) Group found median age 32 years in their study, Guerra et al (2004) reported average age 34.5±11.9 years, and Prasad et al (2013) reported mean age 40 ± 13.6 years in their sampled leprosy cases.

Lepromatous leprosy is an established risk factor for ENL. In present study, majority of the patients belonged to the LL subtype (74.22%), whereas BL, BT and BB were seen in 13.4%, 11.34% and 1.03% of cases respectively. Predominance of LL subtype among ENL patients was also found in the ENLIST study and that by Guerra et al (2004).

More often than not, ENL presents in its classic nodular form and atypical forms like bullous, ulcerated or necrotic forms have been reported in smaller percentage of cases. (Walker et al 2014,

Walker et al 2015) In current study majority of the patients (86.59%) had nodular lesions cases, whereas necrotic and bullous lesions were seen in 19.58% and 13.40% cases respectively.

Even though we had 38 (39.17%) cases that had completed MDT, a high BI of 4 was seen in about half of the cases (51.54%). The ENLIST group had also reported a median BI of 4 and high BI was reported in about 20% of cases of ENL by Guerra et al (2004). This finding stresses upon the importance of estimation of BI in all cases of ENL, particularly in institutional set up. It also tells us that the bacillary load takes a long time to come down even after completion of one year course of MDT and no doubt, a high BI>4 has been universally accepted as a risk factor for the development of ENL.

About one third of the patients who came for consultation for the first time did so when the first episode of ENL occurred; however an almost equal number of patients reported only after the fourth episode. Changing socioeconomic and education status particularly in rural areas has clearly changed the health seeking behavior. However, stigma associated with leprosy still forces a lot of them to come to the health centre at a very late stage.

In present study, about one-fourth of the patients had some co-morbidity with Diabetes mellitus and hypertension being the common ones seen in 11.34% and 7.21% of cases respectively. This could be because of the effect of long term corticosteroid therapy in ENL. However, presence of one case of chronic kidney disease was equally important because recurrent ENL is known to affect the functioning of kidneys in adverse way. We also had 1 HIV positive (PLHA) case (1.03%).

The common systemic association reported in ENL is arthritis, peripheral edema, glomerulonephritis, lymphadenitis, hepatitis and orchitis. Almost all the studies on ENL have reported these associations in moderate to high proportion of cases (Walker et al 2014, Dutta 1979, Prasad et al 2013). Present study has consistent findings with previous studies. Arthritis was present in 79.38% cases, being the most common association followed by peripheral edema and glomerulonephritis in 29.89% cases each. These complications have been reported by others as well (Ponce et al 1989, Vengadakrishnan et al 2004). In some cases hepatitis can be quite severe (Mendiratta et al 2014). Needless to say, severity of these systemic associations had the major contribution towards the morbidity and disability among the patients admitted to our hospital.

Even though ENL is known to be more common in the lepromatous pole where involvement of large nerve trunks is unusual, we had evidence of multiple nerve involvement in many of our cases. 16 of our cases had 3 nerves involved and 6 had even 4 nerves involved. Nerve involvement is central to the pathology of leprosy and it may occur even after the completion of MDT. Moreover, those who have downgraded from high immunity status, such as borderline leprosy, can still have involved nerves. Contrary to traditional belief, ENL can be an important cause of neuritis like Type-1 lepra reaction. In current study, nerve enlargement and tenderness were frequently found (70.1 % and 50.51% respectively) and even palsy was seen in 8 cases. The outcome of our study clearly underscores the importance of nerve examination and prompt treatment in all cases of ENL.

A higher incidence of patients with a high BI of >4 even after completion of one year of WHO - MDT, higher incidence of comorbidities like DM and hypertension and multiple nerve trunk involvement found in our study should act as an alert for treating dermatologists, other treating doctors and public health personnel involved in leprosy care in Odisha. The data from this hospital based

study can not be directly extrapolated to field situations but will serve as a guide for planning such studies.

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