

Peripheral Neuropathy in Leprosy and its Consequences – A Cross-sectional Study in a Tertiary Health Care Center of Bihar

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Leprosy is an ancient bacterial disease that, although curable, continues to be a significant health problem in India. Despite the development and huge success of efficient and cost-effective multidrug therapy (MDT), lack of awareness and social stigma result in delayed reporting of cases. Hence, dermatologists/ leprologists should be more aware and adept in detecting and managing the neural impairments at comparatively earlier stages, as it can prevent chronic disabilities and significantly improve patient's quality of life. Herein, we conducted a single center, cross-sectional study from August 2022 to April 2023 at IGIMS, Patna, a tertiary care center of Eastern India on 126 of leprosy/ Hansen's disease attending Dermatology OPD to understand various presentations and consequences of neuropathies in leprosy. A comprehensive cutaneous, systemic, and neurological evaluation was done. Peripheral nerve functions were assessed clinically and by the means of Semmes monofilament testing as well as nerve conduction studies (NCS). Of the 126 patients included in the study, 87 (69.04%) were males and 39 (30.9%) were females. Ten were classified as tuberculoid Hansen's disease (TTHD), 55 as borderline tuberculoid Hansen's disease (BTTHD), 3 as borderline Hansen's disease (BBHD), 29 as borderline lepromatous Hansen's disease (BLHD), 18 as lepromatous Hansen's disease (LLHD), 6 as pure-neuritic leprosy (PNL) and 6 patients were unclassified. Majority patients belonged to 30 to 39 years age group followed by 40 to 49 years age group. The most common nerve found thickened was ulnar nerve followed by posterior tibial nerve and common peroneal nerve. 46/126 (36.5%) had symptoms for more than a year, 37/126 (29.3%) came with grade 2 disability – both indicate delayed diagnosis and timely treatment. Most common neuropathy encountered was demyelinating sensorimotor neuropathy followed by axonal and demyelinating sensorimotor neuropathy. The present study provides a general picture about the current profile of leprosy especially neural involvement in these cases reporting to this center and highlights the importance of early detection of disease so as to prevent its long term and often irreversible consequences. This study emphasizes the need of community-based research cum interventions for effective and vigorous implementation of awareness about the disease, facilities for investigation, and timely provision of proper therapy for disease and complications.

Keywords: Leprosy, Neuritis, *M. leprae*, Neuropathy, Nerve Conduction Study

Introduction

Leprosy, one of the oldest diseases of mankind,

continues to be a significant health problem in many parts of the world. Though India has

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achieved elimination at public health level (prevalence less than 1/10, 000) in 2005, it continues to be significant health problem with pockets of endemicity and high grade 2 disabilities in several parts of India including Bihar, Chhatisgarh, Jharkhand and Odisha (NLEP 2019, NSP 2023-27). It results from infection with the *Mycobacterium leprae* bacillus which chiefly affects skin and peripheral nerves, causing several sensory, motor, and autonomic impairments. Neural involvement is primarily due to the selective affinity of lepra bacilli for Schwann cells. Neuropathies of leprosy take various forms and shapes. At one end is the cutaneous nerve involvement adjacent to the anesthetic skin patch and the other is of symmetrical pan sensory neuropathy and the devastating sensory ataxia of leprous ganglionitis. Despite the development of effective and curative therapeutics via multidrug therapy (MDT), poor knowledge of disease, barriers in access to health care and disability-related social stigma result in underreporting and reporting delays of cases, leading to overall worsening of the outcome. The aim of this paper is to describe various presentations of disease and consequences of neuropathies in leprosy in cases reporting to IGIMS, Patna, a major government tertiary health care center of Bihar.

Material and Methods

The present study was a single center, cross-sectional study conducted in the Department of Dermatology at Indira Gandhi Institute of Medical Sciences, Patna, India, from August 2022 to April 2023. A total of 126 leprosy patients were included in our study. The sample size is comparable to other observational studies conducted by Badhan et al (2014), Giridhar et al (2012), Gupta et al (2019) and Patel et al (2021). Informed written consent was obtained from all the subjects. The patients were classified based on Ridley - Jopling classification (1966) and Indian classification of leprosy. (Ramu 1981, IAL 1982).

After obtaining detailed history, a complete physical, motor, sensory and nerve examination was done (Jopling & McDougall 1996). A slit skin smear examination was done on all patients and histopathological confirmation was done in doubtful cases. Disabilities were graded by the WHO criteria (Brandsma & van Brakel 2003). All patients received Multi drug therapy (MDT) following the diagnosis. Patients were classified into paucibacillary (PB) and multibacillary (MB) types as per standard criteria of national programme based on number of skin lesions, nerve involvement and slit-skin smears (SSS) for acid fast bacilli (AFB) (NLEP 2019). Paucibacillary patients with no observable bacilli in slit-skin smears were treated for six months with one supervised monthly dose of 600 mg rifampicin and 100 mg dapsone in conjunction with 100 mg/day dapsone; Multibacillary patients with positive slit-skin smears for acid fast bacilli (AFB)/ *M. leprae*, received a monthly supervised dose of 600 mg rifampicin, 100 mg dapsone, and 300 mg clofazimine together with 100 mg/day dapsone and 50 mg/day clofazimine for 12 months (NLEP 2019).

The analyzed components of the neurologic examination were: (i) Clinical examination of bilateral ulnar, bilateral median, bilateral common peroneal nerve and bilateral posterior tibial nerve, (ii) Semmes-Weinstein monofilament test for Sensory NFI assessment, (iii) Voluntary muscle testing for assessing Motor NFI and (iv) Nerve conduction study for assessing severity of sensory-motor dysfunction. (McLeod et al 1975, Chaudhary et al 2023, Patel et al 2021)

Comprehensive clinical examination of bilateral ulnar, bilateral median, bilateral common peroneal nerve and bilateral posterior tibial nerve was done. The nerves were palpated and assessed based on thickness and tenderness, following the grading system used by Sreejith et al. (2021). Grade 1 (mild) indicated nerves

thickened compared to the contralateral nerve. Grade 2 (moderate) referred to rope-like thickening. Grade 3 (severe) denoted nerves that were thickened and nodular/beaded. Thermal sensation was determined using cold metal (15°C) objects, and a safety pin was utilized to ascertain pain perception.

Tactile threshold was tested using Semmes Weinstein monofilaments, as done by Suda et al (2020). These monofilaments vary in thickness and have different values in grams: 1 = 300 g, 2 = 4 g, 3 = 2 g, 4 = 0.2 g, and 5 = 0.05 g. The inability to perceive the touch of any of these monofilaments indicates a lack of tactile sensitivity at that specific pressure.

Large nerve fiber was complementarily evaluated by means of Nerve Conduction Study. NCS were conducted in all the subjects using Nerve Conduction Velocity-Electro Myography (NCV-EMG) machine at the Department of Neurology according to the standardized protocol also utilized by Vashisht et al (2014) and Chaudhary et al (2023). In a nerve conduction study, normal conduction is indicated when nerve conduction velocities (NCV) fall within the typical range of 50-60 meters per second (m/s) for upper limbs and 40-50 m/s for lower limbs, along with amplitudes within the normal range. Reduced conduction is graded based on the extent of deviation from these normal values. Mild reduction is characterized by a slight decrease in NCV (10-20% below normal) and a slightly reduced but still mostly intact amplitude, remaining above 50% of the lower limit of normal. Moderate reduction involves a more noticeable decrease in NCV (20-40% below normal) and a reduction in amplitude to 25-50% of normal. Severe reduction is marked by a significant decrease in NCV (more than 40% below normal) and an amplitude less than 25% of normal or an absent response altogether. These grading criteria assist in assessing the severity of

nerve damage and guiding appropriate treatment interventions.

Inclusion criteria:

A diagnosed patient of leprosy, willing to participate in the study were included in the study.

Exclusion criteria:

Patients with neuropathy due to other causes such as diabetes, hypothyroidism, neuromuscular diseases, HIV, drug induced neuropathy or family history of hereditary neuropathies were excluded from the study.

The study was conducted after obtaining approval from the Institutional Ethical Committee (IEC approval number- S.No 585/IEC/IGIMS/2022).

Results

A total of 126 patients with leprosy were enrolled in the study out of which 87 (69.04%) were males and 39 (30.9%) were females.

The mean age for total patients was 38.4 ± 3.25 years with a range of 8 years to 67 years. Among 126 patients, 10 (7.93%) were classified as tuberculoid Hansen's disease (TTHD), 55 (43.65%) as Borderline Hansen's Disease (BTHD), 3 (2.38%) as borderline Hansen's disease (BBHD), 29 (23.01%) as borderline lepromatous Hansen's disease (BLHD), 18 (14.2%) as lepromatous Hansen's disease (LLHD), 6 (4.76%) as pure neuritic leprosy (PNL) and 5 patients were unclassified referred as Oth (Others) (Table 1).

A total of 118 (93.6%) patients were treated for multibacillary disease (MB) and 10 (7.93%) undertook treatment for paucibacillary leprosy (PB).

Majority patients belonged to 30 to 39 years age group (32.53%) followed by 40 to 49 years age group (25.39%). Vast majority of patients (79, 62.6%) hailed from rural area and 36.5% patients (46 patients) had complaints for more than one year.

Table 1 : Distribution of patients by gender and type of leprosy.

Type of leprosy	Males		Females		Total	
	No.	%	No.	%	No	%
TT	7	5.55	3	2.38	10	7.93
BT	37	29.36	18	14.28	55	43.65
BB	1	0.79	02	1.58	03	2.38
BL	24	19.04	05	3.96	29	23.01
LL	13	10.31	05	3.96	18	14.2
PNL	03	2.38	03	2.38	06	4.76
Oth	02	1.58	03	2.38	05	3.96
Total	87	69.04	39	30.95	126	100.0

Table 2 : The presenting symptoms including neuropathies in leprosy patients included in the study (Total-126).

Presenting symptoms	Patients	%
Anesthetic patch	78	61.9
Hypoesthetic patch	65	51.5
Tingling sensation	67	53.1
Trophic ulcer	32	25.3
Paresthesia	76	60.3
Spontaneous blister	15	11.9
Claw hand	11	8.7
Foot drop	15	11.9
Resorption of digits	1	0.79
Bilateral pedal edema	31	24.6
Erythema nodosum leprosum	52	41.2
Nasal congestion	8	6.3
Leonine facies	2	1.5
Muscle atrophy	19	15.0
Anhidrosis	2	1.58
Type 1 lepra reaction	13	10.3

It may be noted that several patients had presented with more than one symptom.

The predominant symptoms at the time of diagnosis were related skin symptoms i.e. anesthetic or hypo-esthetic patch followed by nerve symptoms i.e. tingling sensation,

paresthesia, or claw hand. A significant proportion of patients presented with leprosy reactions (41.26%) (Table 2).

A total of 38 patients had ocular complaints at the time of presentation. Major ophthalmic complaints encountered in our patients was impaired lid closure (17) followed by madarosis (9) and decreased corneal sensations (8). Corneal ulcers and cataract were also seen in small subset of patients. Patients were promptly referred to Regional Institute of Ophthalmology OPD for adequate treatment.

Bilateral ulnar, bilateral median, bilateral common peroneal nerve, and bilateral posterior tibial nerve of all the patients were examined for nerve thickness. Total 1008 nerves were examined out of which 264 (26.1%) nerves were found thickened. The most common nerve found

thickened was the ulnar nerve with 146 (57.9%) thickened nerves, followed by 48 (19%) posterior tibial nerve, 38(15.1%) common peroneal nerve and 32 (12.6%) median nerve was found to be thickened.

Tactile threshold was tested with Semmes Weinstein monofilaments and decreased threshold was seen in 90% patients of TTHD, 87.2% of BTHD, 33.3% of BBHD, 62.1% of BLHD, 61.1% of LLHD and in 50% patients of PNL (Fig.1).

Nerve conduction study was done on all patients and 67 patients (53.1%) had normal conduction levels. Bilateral median, bilateral ulnar and bilateral sural nerves were studied in nerve conduction study. Most common neuropathy was demyelinating sensorimotor neuropathy followed by axonal and demyelinating sensorimotor neuropathy. Only four patients had pure axonal senso-

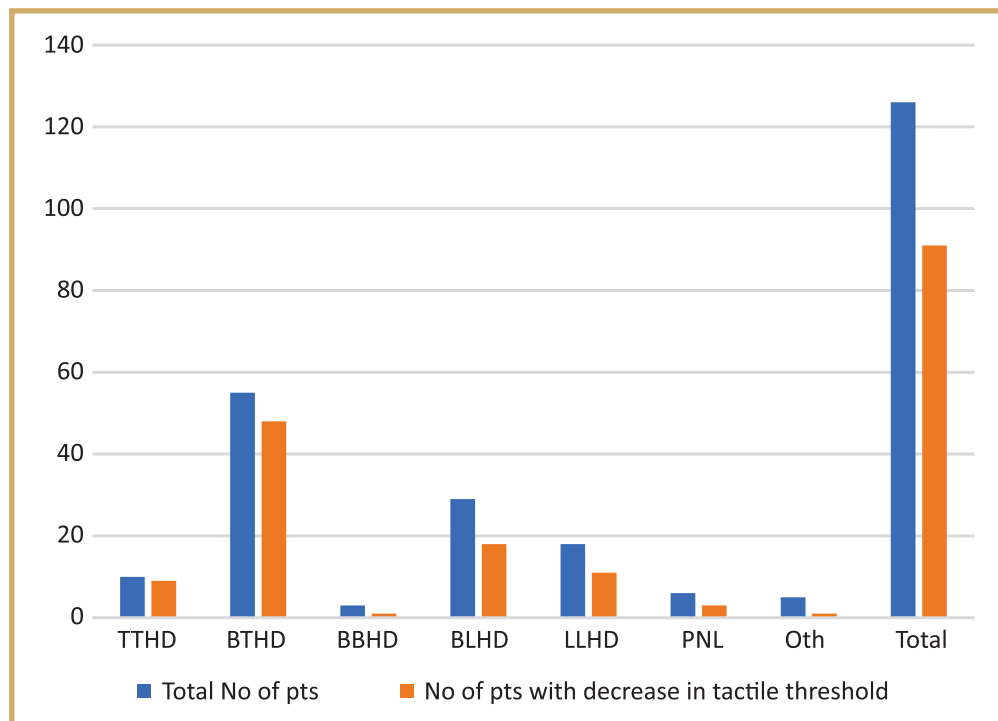


Fig. 1: Sensory impairment in different types of leprosy.

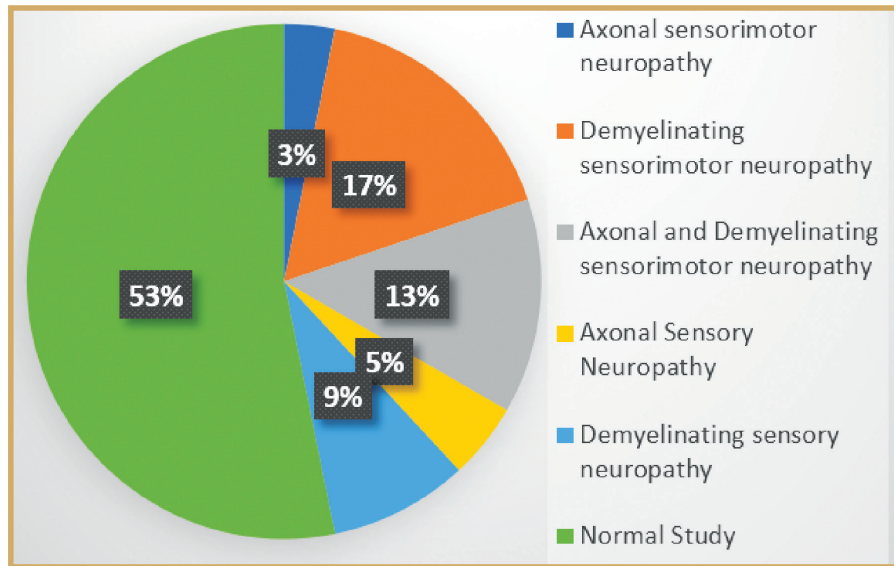


Fig. 2: Type of neuropathy as per electrophysiological diagnosis.

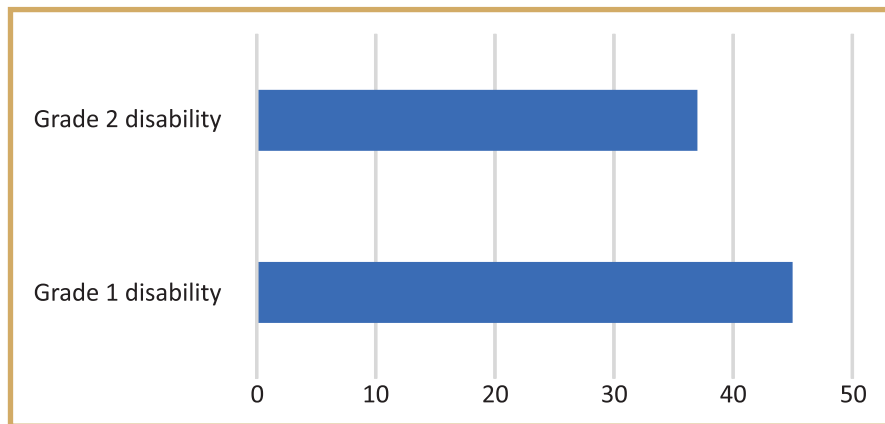


Fig. 3: Types of disabilities seen in the patients studied.

rimotor neuropathy. Complete electrophysiological profile is summarized in Fig. 2.

After analyzing outcomes of clinical examination, monofilament testing and nerve conduction study it was concluded that, out of 126 patients, 94 patients either presented with nerve symptoms or had co-existent nerve and skin involve-

ment. Among them, majority presented with disability (65%) followed by mononeuropathy (40.42%), polyneuropathy (19.14%), mononeuritis multiplex (11.7%), and autonomic neuropathy (2.12%).

A total of 82 patients (65%) presented with disabilities. This contrasts with study done by

Table 3 : Demographic characteristics of patients presenting with disability.

	Trophic ulcer	Claw hand	Foot drop	Resorption of digit	Muscle atrophy	Leonine facies
Age group(years)						
0-9		1				
10-19	1				1	
20-29	1				3	
30-39	4	3	2	1	4	
40-49	6	3	6		4	
50-59	9	2	4		5	
>60	11	2	3		2	2
Sex						
Male	21	4	9		12	1
Female	11	7	6	1	7	1
H/O prior MDT Intake						
Yes	9	1	3		4	2
No	23	10	12	1	15	
Bacteriological index						
≤3 +	14	4	6		7	1
>3 +	18	7	9	1	12	1

Table 4 : Disabilities seen in different types of Hansen's disease.

Disabilities	TTHD	BTHD	BBHD	BLHD	LLHD	PNL
Anesthetic patch	7	38	1	27	5	
H/O Spontaneous blister	3	6				
Trophic ulcer				13	17	2
Claw hand		4	1	3	3	
Foot drop				6	7	2
Muscle atrophy		2		8	6	3
Resorption of digits						1
Leonine facies				1	1	

Raghavendra et al (2017), Praveena et al (2023) and Williams et al (2019) where proportion of leprosy patients with disability was lower. Among 126 patients, 45 patients (35.7%) presented with Grade 1 disability and 37 patients (29.3%) presented with Grade 2 disability (Fig. 3).

The disability was higher in males as compared to females and the deformities in the feet were most common followed by hand and face. The complete demographic profile of the patients presenting with disability is described in Table 3.

Also, when analyzed in relation to the types of Hansen's disease, it was noted that disabilities were more frequent in borderline lepromatous leprosy followed by borderline tuberculoid leprosy (Table 4).

Several patients presented with more than one complaint. Only 38 (30.1%) patients presented within 6 months of onset of symptoms.

Discussion

In the history of modern medicine, in terms of physical disabilities and stigma, leprosy is one of the most important diseases. Major factors associated with it include illiteracy, perceived economical inadequacy, need for change of occupation due to leprosy and the perception of leprosy as untreatable, crippling disease (Somar et al 2020). Neuropathy and related disabilities are the major long-term consequences of leprosy, which remains a global medical concern. *Mycobacterium leprae* has a distinct predilection for areas of low body temperature and has a unique tropism for nerves. This is due to the selective affinity of lepra bacilli for Schwann cells. Neuropathies of leprosy take various forms and shapes (Chaudhary et al 2023). These range from the local cutaneous nerve involvement adjacent to the anesthetic skin patch to symmetrical pan sensory neuropathy and the devastating sensory ataxia of leprous ganglionitis (Khadilkar et al 2021).

Despite of leprosy being in post elimination era, new cases continue to be reported from different parts of India (NSP 2023-2027). Globally, the registered prevalence of leprosy (number of cases on treatment at the end of 2021) was 133802, and the prevalence rate was 16.9 per million population. Out of this, India alone accounted for 75394 (56.3%) cases (WHO 2022).

In the last two decades, significant advancements have been made in the treatment of leprosy. With the advent of multi-drug treatment (MDT), the prevalence of leprosy decreased over the

decades. Although the patients who completed treatment were considered bacteriologically cured of *M. leprae* infection, still the nerve damage caused by *M. leprae* leaves many patients with impaired sensation and physical deformities. With persistent efforts towards prevention and treatment, the numbers of new cases diagnosed per year have been decreasing, but leprosy exists in many parts of the world and is still endemic in some regions.

The male-to-female ratio in the present study was 2.23:1. Other studies showed a similar ratio of 2.37:1 (Kalita et al 2020), 2.5:1 (Badhan et al 2014), 3.5:1 (Giridhar et al 2012) and 1.7:1 (Thakkar & Patel 2014) thereby showing higher proportion of males as compared to females presenting with leprosy. This trend is known for ages. The lower prevalence of females could be because of lesser medical care sought by the females due to gender bias and because of the social stigma attached to the disease. Higher frequency among males possibly indicates their more vulnerability because of greater mobility and increased opportunities for contact in big population.

The age of the patients ranged from as young as 8 years to as old as 67 years in our study. Majority of patients belonged to the age group of 30-39 years i.e. productive phase of life. Similar observations were also made by other researchers (Giridhar et al 2012, Gupta et al 2019, Kumar et al 2020, Praveena et al 2023). Increased incidence in this group indicates vulnerability because of greater mobility, increased opportunity for contact in big population and long incubation of disease). In addition, these groups having high motivation for health seeking behavior. This contrasts with study done by Jindal et al (2021) and Patel et al (2021) which showed maximum patients in 15-29-year age group and 18-30-year group respectively.

Clinically, MB (Multibacillary) cases clearly outnumbered PB (Paucibacillary) cases with a



Fig. 4: Resorption of digits (Grade 2 disability).



Fig. 5: A thickened greater auricular nerve is observed adjacent to a patch on the cheek.

ratio of 14.8:8. Similar observations have been made by all in the above studies. It was also found that multibacillary disease was more commonly diagnosed in the patients hailing from rural area. This is possibly due to the inaccessibility of rural population to medical facilities for early diagnosis and treatment of disease.

A total of 69% of our patients were in the borderline category (includes borderline tuberculoid, borderline lepromatous and mid borderline disease) while 14.2% had lepromatous leprosy, 7.93% had tuberculoid leprosy and only 4.76% presented to us with pure neuritic leprosy. Borderline cases have become more common after introduction of multidrug therapy as opposed to the polar forms of the disease being more commonly seen in the dapsone era. The low percentage of polar forms of leprosy is like observations by Jindal et al (2021), Patel et al (2021), Kumar et al (2020).

Skin lesions were the most common presenting complaint in patients (93.6%). Majority of patients

presented with anesthetic or hypo esthetic patch, mostly distributed on extremities (upper limb and lower limbs), in asymmetrical fashion (90%) and with associated hypopigmentation (87.6%). Leptra bacilli preferentially involve those areas of skin which have a relatively lower temperature and are more exposed to trauma. This explains why the lesions are predominantly seen in extremities. In our study, cutaneous complaints were followed by neurological complaints such as tingling sensation, numbness, paresthesia, and slippage of footwear unknowingly in 53.1% of patients. This contrasts with studies done by Uiquey et al (2019, 15.6%) and Thakkar & Patel (2014, 35.3%) where nerve involvement is seen in minority of patients. This might be explained by the fact that most of our patients had poor socio-economic status, leading to delay in seeking health care. Other presenting features were trophic ulcer in 32 (25.3%), erythema nodosum leprosum in 52 (41.2%), bilateral pedal edema in 31 (24.6%) patients, deformities including resorption of fingers (Fig.4).

In the present study, the most common nerve found to be thickened was the ulnar nerve (57.9%), followed by the posterior tibial nerve and common peroneal nerve. Many patients had grade 2 thickening (69%) followed by grade 1 and 3. Vashisht et al (2014) and McLeod et al (1975), also reported the ulnar nerve as the most affected nerve. A very rare case of greater auricular nerve involvement adjacent to patch over face was also reported (Fig. 5).

Tactile threshold was tested with Semmes Weinstein monofilaments. These monofilaments vary in thickness, with a different value in grams for each one (1 = 300 g, 2 = 4 g, 3 = 2 g, 4 = 0.2 g, and 5 = 0.05 g), and the inability to perceive the touch of even one of them represents an absence of tactile sensitivity to that given pressure. Decreased threshold was seen in 90% patients of TTHD, 87.2% of BTHD, 33.3% of BBHD, 62.1% BLHD and 61.1% of LLHD and in 50% patients of PNL. A nerve conduction study was done on all the patients and the most common neuropathy found was of demyelinating sensory and sensorimotor type. This was coherent with study done by Patel et al (2021).

After analyzing outcomes of clinical examination, monofilament testing and nerve conduction study it was concluded that, out of 126 patients, 94 patients either presented with nerve symptoms or had co-existent nerve and skin involvement. Nerve conduction studies are important to detect nerve impairment and diagnose the type of nerve involvement (Chaudhary et al 2023). Among the cases with nerve involvement, the majority presented mononeuropathy (40.42%) followed by trophic ulcer (34.04%), polyneuropathy (19.14%), mononeuritis multiplex (11.7%), disability (28.72%) and autonomic neuropathy (2.12%) (Fig. 2).

A total of 82 patients presented with disabilities (65%). This contrasts with data published

by Raghavendra et al (2017), Praveena et al (2023) and Williams et al (2019). Illiteracy, lack of awareness and very high social stigma can be held accountable for such large cases of disabilities among leprosy patients of Bihar. Among 126 patients, 45 patients (35.7%) presented with Grade 1 disability and 37 patients (29.3%) presented with Grade 2 disability. The most visible common deformity was trophic ulcer of hands and feet followed by foot drop and claw hand.

The disability rate was higher in males as compared to females and the deformities in the hand were most common followed by feet and face. The complete demographic profile in patients presenting with disability is described in Table 3. Also, when correlated with the types of Hansen's disease, it was noted that disabilities were more frequent in borderline lepromatous leprosy followed by borderline tuberculoid leprosy (Table 4).

Several patients presented with more than one complaint. Only 38 (30.1%) patients presented within 6 months of onset of symptoms which can be attributed to illiteracy and communication gap among patients, especially of Eastern India. Hence, leprosy awareness and programmes aimed at elimination need to be more vigorously implemented targeting these sections.

The proportion of patients with grade 1 disability was higher than with grade 2 disability. At National level to assess program effectiveness only grade 2 disability record is maintained but for prevention of disability, grade-1 assessment is more important. Because, before visible deformity (grade-2) occurs, nerve function impairment occurs (sensory, motor or both) i.e. those patients with G2D must have passed through the stage of grade-1. Therefore, while examining any leprosy case, after examination of skin lesions, thorough neurological examination of peripheral nerves is essential. For this,

assessment of sensory NFI, motor NFI are needed along with nerve palpation for thickening, tenderness, and reactions for detection of grade-1 disability. The most important factor to prevent disability in leprosy patients is early detection and adequate treatment of neural impairment. Registration delay is recognized as a risk factor for disability in leprosy, but this is the result of complex interactions between physical, social, economic, and psychological factors. Hence, leprosy awareness and programmes aimed at elimination need to be more vigorously implemented.

Conclusion

The present study gives a general picture about the current trends of profile of leprosy in this region reporting to a tertiary care center and highlights the importance of early detection of disease to prevent its long term and often irreversible consequences. This study emphasizes the need for effective and vigorous implementation of awareness about the disease, facilities for investigation, and unhindered provision of therapy. Newer strategies to target population groups at higher risk need to be devised to achieve complete eradication of this menace from society.

Limitations

Main limitation of our present study is its being cross-sectional analysis, hence follow up of the patients was not done. Further studies are required to gain in depth knowledge regarding long term consequences and possible treatment modalities to halt the progression of the disease. Such information will help in better planning for preventive measures, early diagnosis, and management. The sample size is comparable to other observational studies conducted by Badhan et al (2014), Giridhar et al (2012), Gupta et al (2019) and Patel et al (2021). Also, as our study was conducted in a tertiary care hospital, it is not likely to be representative

of the situation on the field and should be complemented by community-based strategies from catchment areas. Still, it gives a general picture of the current trends of leprosy in our region based on which prospective studies can be planned in the field.

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