The Clinical, Neurophysiological, Radiological and Neuropathological Study of Hansen's Disease in Hamidia Hospital Bhopal

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ABSTRACT

Introduction: The peripheral nerve injury has been associated with physical disability and is the most serious complication of leprosy. The diagnostic tests including nerve conduction velocity testing and ultrasound of ulnar nerve may reveal the defect in the nerve before the disease become clinically more apparent.

Material and methods: The study was an observational study with a total of 50 patients. Patients who were diagnosed cases of leprosy are registered in this study based on inclusion and exclusion criteria.

Results: The most frequent clinical forms were borderline tuberculoid (46%) and indeterminate (14%) and borderline number (14%). Regarding the degree of disability 78% had leprosy grade 0, 18% had grade 1 and 4% had grade 2. With nerve conduction study, the changes in sensory nerve conduction were more pronounced. high resolution ultrasonography of the ulnar nerve at elbow was done showed nerve thickening in 54% cases and 10% of the patients showed atrophic changes. Out of the 26 patients who undergone sural nerve biopsy acid fast bacilli was found in 7 patients; mononuclear infiltrates in 24 patients, thickness of endo-peri-epi-neurium was found in 5 patients.

Conclusions: Sonography and electrophysiology were complementary for identifying ulnar nerve neuropathy in patients with leprosy, this reinforces the role of sonography in the investigation of leprosy ulnar neuropathy. Nerve conduction testes can reveal nerve involvement before the disease became clinically apparent.

Keywords: Leprosy, Nerve Conduction Study, Sural Nerve, Biopsy, Ulnar Nerve, Ultrasonography, Hansen's Disease, Neuropathy, Sensory Nerve, Skin

INTRODUCTION

Leprosy, also known as Hansen's disease (HD), is long term infection caused by the bacilli mycobacterium leprae and Mycobacterium lepromatosis.^{1,2} Initially, infections are without symptoms and typically remain this way from 5 to 20 years.² Symptoms that develop include granulomas of the nerves, respiratory tract, skin, and eyes.2 This may result in a lack of ability to feel pain and thus loss of parts of extremities due to repeated injuries or infection due to unnoticed wounds Leprosy occurs more commonly among those living in poverty. Globally in 2012, the number of chronic cases of leprosy was 189,000, down from some 5.2 million in the 1980s.²⁻⁵ The number of new cases was 230,000.² Most new cases occur in 16 countries,^{2,3} with India accounting for more than half. Leprosy was not a specified disease in the Millennium Development Goals (MDGs), but improvements in the other areas they cover, such as education and levels of poverty will help leprosy patients and services, so there is a need to find out newer diagnostic tests that can aid in early diagnosis and proper treatment before the disease can come up with full blown status with disability. There is also a need to study clinical outcomes and to find out

the group of people more affected with the disease, to find out association with the literacy and working habits. The peripheral nerve injury has been associated with physical disability and is the most serious complication of leprosy. The diagnostic tests including nerve conduction velocity testing and ultrasound of ulnar nerve may reveal the defect in the nerve before the disease become clinically more apparent.

Study Objectives were to evaluate the clinical profile of Hansen's disease with respect to sensory involvement, thickness of ulnar, affected nerves, skin lesions, lepra reactions, to compare the sensory involvement of ulnar and median nerves of both upper limbs, to evaluate the characteristic changes in ulnar nerve by ultrasound of ulnar nerve at elbow and to compare the nerve biopsy finding of sural nerve in different groups.

MATERIAL AND METHODS

This was an Observational study of two years, carried out at Hamidia hospital Bhopal in Madhya Pradesh, a Tertiary Centre where patients are referred and being treated. Data collected with patients coming in OPD. Patients were being recruited for the study who were diagnosed case of Hansen's disease. Patients undergone nerve conduction study, ulnar nerve high resolution sonography, nerve biopsy and clinical assessment. Study was done after due ethical clearance and informed consent.

Inclusion criteria

Patients were being recruited for the study who were diagnosed case of Hansen's disease.

Exclusion criteria

Patients at risk of a neuropathy other than leprosy, i.e. diabetes, alcoholism, risk group for HIV infection; patients with a family history of hereditary neuropathy, and patients over 60 years of age.

Method: The variables of age, sex, education, number of skin lesions, number of affected nerves, operational classification, clinical forms of the disease and disability degree, nerve conduction velocity test of ulnar nerve, ultrasound and nerve biopsy findings. The assessment of degree of disability was performed according to current classification system of WHO; using following criteria: grade 0 indicates no loss of sensitivity or visible deformity; grade 1 defined by loss of sensitivity without visible deformity and grade 2 indicates presence of

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How to cite this article: T.N. Dubey, Neelesh Damor. The clinical, neurophysiological, radiological and neuropathological study of hansen's disease in hamidia hospital Bhopal. International Journal of Contemporary Medical Research 2017;4(6):1273-1275.

visible deformity. Grades 1 and 2 were considered as disability. For electrophysiological study diagnosed cases of pauci and multibacillary leprosy as well as the freshly diagnosed ones were selected. There were 27 males and 23 females in the study age group 15-60 years. Informed consent was taken from all the patients and after obtaining a brief history regarding the onset of their symptoms and treatment taken, if any. They were subjected to a thorough clinical examination.

The electrophysiological nerve conduction assessment was done for all the patients using RMS machine. The sites for stimulation for median and ulnar nerve were wrist and the elbow and the recording sites were motor point of abductor pollicis brevis muscle and abductor digiti minimi respectively. Reference electrode was placed distally over first metacarpophalengeal joints for median nerve and over 5THmetacarpophalengeal joint for ulnar nerve.

Patients' also undergone ultrasound of ulnar nerve at the elbow joint and sural nerve biopsy was performed after written consent.

STATISTICAL ANALYSIS

Descriptive statistics like mean and parentage calculation was done for data interpretation.

RESULTS

50 patients of leprosy were assessed for disability degree, including 46% female and 54% males (table 1). The mean age

Variables	N	Percent age (%)		
Age groups(yrs)				
15-30	14	28%		
31-60	36	72%		
Sex				
Female	23	46%		
Male	27	54%		
Education level(yrs)				
0-4	19	38%		
5-8Th	16	32%		
≥9	15	30%		
Skin lesions				
≤5	45	90%		
>5	5	10%		
Affected nerves				
≤2	27	74%		
>2	13	26%		
Who classification				
Paucibacillary	42	84%		
Multibacillary	8	16%		
Lepra reaction				
No	41	82%		
Yes	9	18%		
Clinical forms				
Indeterminate	7	14%		
Borderline tuberculoid	23	46%		
Borderline	8	16%		
Lepromatous	12	24%		
Degree of disability				
Grade 0	39	78%		
Grade 1	9	18%		
Grade 2	2	4%		
Table-1: Characteristics of leprosy cases				

of the patients was 38.8 years with median age of 38 years. Majority of the patients has low education; 38% had between 0-4 years education, 32% had education between 5-9 years and 30% above \geq 9 years (table 1). 74% of the patients had more than two nerves involved. According to the operational classification, there was a Prevalence of Paucibacillary disability 10.88% (table 2). In most of the cases 82% had no leprosy reaction. The most frequent clinical forms were borderline tuberculoid (46%) and indeterminate (14%) and borderline number (14%). Regarding the degree of disability 78% had leprosy grade 0, 18% had grade 1 and 4% had grade 2. When nerve conduction tests were done, it showed reduced conduction velocities besides changes in latency and amplitude in the affected nerves (table 3 and 4). The changes in sensory nerve conduction were more pronounced. Also, sensory latencies and amplitude changes were more severe than motor latencies and amplitude in those presents with muscle palsy. Nine of our patients were in Type 2 Lepra reaction while the rest had no such complaints. When examined for sensory impairment of touch, pain, temperature 10 of the patients complained of impaired sensation over corresponding neural distribution. Cranial nerve function was found to be normal in all the patients. Nerve conduction assessment revealed gross impairment of the conduction velocities, latencies and amplitude in all the patients consistent with the clinical findings of Hansen's disease. When high resolution ultrasonography of the ulnar nerve at elbow was done showed nerve thickening in 54% cases and 10% of the patients showed atrophic changes. None of the patients showed other ultrasonography findings like fibrosis or vascularization. On comparing the above-mentioned

Variables		Disability	
Age groups (yrs)	N	Yes (%)	No (%)
15-30	14	2(14.28)	12(85.71)
31-60	36	9(25)	27(75)
Sex			
Female	23	5(21.73)	18(78.26)
Male	27	6(22.22)	21(77.77)
Education level (yrs)			
0-4	19	4(21.05)	15(78.94)
5-8Th	15	3(20)	12(80)
≥9	16	4(25)	12(75)
Skin lesions			
≤5	45	7(15.55)	38(84.44)
>5	5	4(80.0)	1(20.0)
Affected nerves			
≤2	27	10(37.03)	17(62.96)
>2	23	0(0.0)	23(100)
Who classification			
Paucibacillary	42	4(9.52)	38(90.47)
Multibacillary	8	7(87.5)	1(12.5)
Lepra reaction			
No	41	3(7.3)	38(92.68)
Yes	9	8(88.88)	1(11.11)
Clinical forms			
Indeterminate	7	1(14.28)	6(85.71)
Tuberculoid	23	0(0.0)	23(100.0)
Borderline	7	1(14.28)	6(85.71)
Lepromatous	12	9(75.0)	3(15.0)
Table-2: Clinical factors	associated wit	h the occurence	e disabilitiy
i	n leprosy patier	nts	

Type of leprosy	Amplitude	Velocity	Latency		
	reduced	reduced	increased		
Paucibacillary	10	9	9		
Multibacillary	6	4	3		
Table-3: Showing changes in amplitude, velocity and latency in					
unlar nerve					

Type of leprosy	Amplitude reduced	Velocity reduced	Latency increased		
Paucibacillary	5	5	5		
Multibacillary	5	5	5		
Table-4: Showing changes in amplitude, velocity and latency in					
median nerve					

findings with who class; 23 patients had Paucibacillary that was much more as compared to multibacillary leprosy which are just 4. Neural involvement in multibacillary was found to be clinically less. Out of the 26 patients who undergone sural nerve biopsy acid fast bacilli was found in 7 patients; mononuclear infiltrates in 24 patients, thickness of endo-peri-epi-neurium was found in 5 patients. Neuritis was the most common finding presented in the study.

DISCUSSION

The main factors associated with the development of disabilities in patients with leprosy were the number of affected nerves, leprosy reactions, operational classification and the clinical form of the leprosy.

Peripheral nerve injury has been associated with the physical disability and is the most serious complications of leprosy. Regarding operational classification there was a high rate of MB patients as observed in other studies. These high number suggest a late diagnosis, which may be due to difficult access to health care.

Higher level of education has been considered a determining factor for disease improvement as well as protective factor for the occurrence of disability among leprosy patients. It is well known that sensory nerves are first to be affected in leprosy.⁶ Hence for early detection of leprosy, sensory nerve conduction parameters need to be measured.

The sensory fibers are damaged earlier than motor fibers in leprosy; therefore, in the early stages of nerve damage, it is the sensory fibers that slow a greater quantum of impaired conduction velocities when compared with those in motor fibers.7 Careful clinical testing is useful, but can only detect the presence of neuropathy. However, if neuropathy is found, there already is a Substantial amount of nerve damage. Nerve conduction studies may improve early detection strategies. Peripheral nerves are often enlarged in leprosy, and these are more accurately assessed by US than by clinical palpation. Examination which is limited to defined segments. One of the three key signs of leprosy are the presence of enlarged nerves. Ascertaining the presence of enlarged nerves can be difficult, and for some nerves this is impossible because of their location. Nerve biopsy segments taken from sural nerve showed neuritis as most common presentation. Whatever may be the stage of leprosy, it is the most common finding. Showing mild inflammatory changes tends to continue. Acid fast bacilli can also be seen in the biopsy segments when the bacterial load is high in nerves.

CONCLUSION

Better knowledge of the factors associated with the onset of disability due to leprosy is useful for disability prevention programs and can allow the progression of the disease to the monitored more clearly.

Sonography and electrophysiology were complementary for identifying ulnar nerve neuropathy in patients with leprosy, with clinical symptoms as the reference standard. This reinforces the role of sonography in the investigation of leprosy ulnar neuropathy.

Sural nerve biopsy in experienced hands is safe and that it has revealed pathological changes of significance in this group of patients. Furthermore, the procedure should certainly not replace the examination of well selected and processed skin biopsies, together with the use of routine slit-skin smears in the diagnosis and classification of this disease.

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Source of Support: Nil; Conflict of Interest: None

Submitted: 15-05-2017; Accepted: 20-06-2017; Published: 30-06-2017