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Original Article

Demographic, clinical and histopathological spectrum of leprosy: a study of 30 Pakistani patients

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Abstract

Methods We selected 30 new and previously untreated cases of leprosy that presented at Marie Adelaide Leprosy Center, Karachi, from January 01, 2016 to July 31, 2016 and were diagnosed by a senior leprologist. Information on demographic, clinical and histopathological features of each patient was then collected from the medical records.

Results Mean age of presentation was 36.47±17.57 years with age range of 07-69 years. Male to female ratio was 3.2:1. History of a household contact was positive in 11 (37%) cases. Ulnar nerve was the most common nerve enlarged (83%) and borderline lepromatous leprosy was the most common type of disease.

Conclusion Leprosy is still prevalent in Pakistan. Active case detection and awareness of doctors and community should be done for early diagnosis to prevent disabilities.

Key words
Leprosy, clinical features, histopathology, bacillary index, granulomatous disorder, nerve enlargement, MALC.

Introduction

Leprosy is a chronic infectious and granulomatous disease, caused by *Mycobacterium leprae*. It mainly affects the skin and peripheral nerves and may cause complications like deformities, disabilities and blindness. In Pakistan, it is also known as *Juzam* (Arabic) or *Korrh* (Hindi).[1]

The Ridley-Jopling classification divides the disease into five groups, based upon the cell-mediated immunity (CMI) of the host, bacillary load, and by the delay before diagnosis. At the tuberculoid end of the spectrum (TT), CMI is high and bacillary multiplication is restricted to one or few sites in the skin and peripheral nerves. At the opposite lepromatous pole (LL), CMI is low and there is a hematogenous spread of bacilli to cool, superficial sites e.g. the ear lobes, eyes, upper respiratory mucosa, skin, small muscles and bones of the face, hands and feet, nerves and testes.[2] In the middle are the three borderline types, borderline-tuberculoid (BT), mid-borderline (BB) and borderline-lepromatous (BL). These are immunologically unstable and at risk of developing immune-mediated lepra reactions.[1]

The leprosy elimination goal set by the World Health Organization (WHO), i.e. a global prevalence rate <1 patient per 10,000 population, was achieved in the year 2000, but

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more than 200,000 new case patients are still reported each year, particularly in India, Brazil, and Indonesia.[3] In terms of leprosy prevalence, Pakistan is considered to be a low endemic country. In the year 2014, a total of 501 new cases were detected in the country. Out of these, 7% were children, 50% were females and 73% were multibacillary. A significant proportion of 18% had a visible deformity (grade-2 disability), at the time of diagnosis.

Marie Adelaide Leprosy Centre (MALC), Karachi and Aid to Leprosy Patients (ALP)/ Rawalpindi Leprosy Hospital are the two major referral hospitals in the country. We analyzed the data of newly diagnosed patients of leprosy in MALC, Karachi.

Methods

We selected 30 new and previously untreated cases of confirmed leprosy that presented at MALC, Karachi, from January 1 to July 31, 2016 and were seen by a senior doctor, experienced in the diagnosis and management of leprosy. All cases that were previously treated or were new but not seen by a senior leprologist, were excluded from the study.

Information on demographic, clinical and histopathological features of each patient was then collected from the medical records, both from the outpatient department, as well as, from the indoor admission records of those who were admitted. Skin biopsies were taken and histopathology done at PNS Shifa Hospital, Karachi

Results

Mean age of presentation was 36.47±17.57 years

with age range of 7-69 years. 2 (7%) out of the total 30 cases were children (**Table 1**). The youngest was a 7-year-old male, followed by a 9 year-old female. There were 2 males in the >65 year age-group; the eldest among these was 69-year-old. Among males, a total of 10 (44%) cases belonged to the 25-44 age-group. Among females, 3 (43%) were in the 15-24 age-group. Out of the total 30 cases, 23 (77%) were males and 7 (23%) were females, with M: F of 3.2:1.

Residence and ethnic background

25 (83%) cases were from Sindh province and 5 (17%) were from Baluchistan. 19 (63%) had their residence in Karachi. Out of the 5 cases from Baluchistan, 4 belonged to Awaran, a remote area in Makran, indicating the clustering pattern of the disease. **Table 2** shows the mother tongue of study population, representing all major ethnic groups of Pakistani population.

Table 1 Ag and sex distribution of study population (n=30).

Age (years)	*Male*	*Female*	*Total*
0-14	1	1	2 (7%)
15-24	4	3	7 (23%)
25-34	5	1	6 (20%)
35-44	5	0	5 (17%)
45-54	2	2	4 (13%)
55-64	4	0	4 (13%)
≥65	2	0	2 (7%)

Table 2 Mother tongue of the studies population (n=30).

Mother-tongue	*N (%)*
Urdu	6 (20%)
Balochi	6 (20%)
Pashto	4 (13%)
Punjabi	3 (10%)
Seraiki	3 (10%)
Bengali	3 (10%)
Hindko	2 (7%)
Sindhi	1 (3%)
Thari	1 (3%)
Brahvi	1 (3%)

Table 3 Presenting symptoms and findings on physical examination (n=30).

	N (%)
Signs/symptoms	
Erythematous lesions	7 (23)
Hypopigmented patches	6 (20)
Loss of sensation in hands, feet	6 (20)
Nerve pain, paresthesia	6 (20)
Nasal stuffiness, epistaxis	5 (17)
Crops of painful nodules	3 (10)
Loss of sensation in lesions	3 (10)
Muscle weakness in hands	3 (10)
Blisters, ulcers in hands, feet	2 (7)
Nodules on ears	1 (3)
Testicular pain, swelling	1 (3)
Types of lesions	
Loss of sensation in lesions	11 (37)
Erythematous plaques, patches	10 (33)
Punched-out plaques	9 (30)
Hypopigmented patches, macules	8 (27)
Bilateral madarosis	7 (23)
Ulcers in hands, feet	7 (23)
Edema feet	5 (17)
Papules, nodules	4 (13.3)
Diffuse infiltration	4 (13.3)
Crops of painful erythematous nodules	3 (10)
Hanging ear lobes	2 (6.7)
Leonine facies	1 (3.3)
Uveitis	1 (3.3)
Collapsed nasal bridge	1 (3.3)
Loss of fingers	1 (3.3)
Orchitis	1 (3.3)

Table 4 Presenting symptoms and findings on physical examination (n=30).

Enlarged nerves	*N (%)*
Ulnar	25 (83)
Common peroneal	21 (70)
Radial cutaneous	18 (60)
Posterior tibial	15 (50)
Great auricular	5 (17)
Median	2 (7)

Occupation and socio-economic status

Occupation ranged from 3 farmers and a vegetable seller to 2 government schoolteachers. There were 2 persons belonging to the armed forces and 1 policeman. There were 2 drivers, 1 mason, 1 welder, 1 carpenter and 1 woodcutter. Two Bengali speaking brothers and their 9-year old sister were madrassa students.

Household contacts

History of a household contact was given in 11 (37%) cases. In 4 (36%) of these cases, it was a parent and in another 4, a sibling. Three had other close family contacts.

Initial signs/symptoms and types of cutaneous lesions

Table 3 shows the signs and symptoms and type of lesions. Patients presented with a variety of cutaneous symptoms and types of lesions. 2 (7%) cases had no visible skin lesions and were therefore classified as having neural leprosy. Bilateral madarosis and ulcers in hands and feet were common features. In most cases, ulcers were caused by burn injuries in anesthetic limbs. Nerve pain, paresthesia were reported by 20 % of cases. Nasal stuffiness, epistaxis and edema feet were also frequent.

Ulnar nerve was the most frequent enlarged nerve followed by common peroneal, radial cutaneous and posterior tibial (**Table 4**). There was no peripheral nerve enlargement found in 1 case

Loss of sensations

Loss of sensation was found in skin lesions in 11 (37%) cases. In 4 of these cases, lesions on the face were found to be anesthetic and in 2 cases, anesthesia was present in lesions on the trunk. In 2 patients, there was a typical glove and stocking pattern. 13 (43%) cases had anesthesia in hands and 8 (27%) in feet.

Muscle weakness

Muscle weakness was detected in the hands of 16 (53%) cases. Wasting of small muscles of hands was seen in 6 (20%) cases. Claw hands were present in 4 (13%) cases and claw toes

were found in 1. Lagophthalmos due to facial nerve damage was found, in the left eye of 1 patient.

Bacterial index (BI)

Slit-skin smears were not taken in the 2 child cases. Among 30 cases, BI was positive in all 6 (100%) patients of LL, 1 cases out of 9 (11.1%) of BL, 2 out 8 of cases of BB (25%) and 1 out of 6 cases of BT (16.6%).

Histopathology

Skin biopsy was taken in 12 (40%) cases and rest of the cases were classified and managed on clinical grounds. Out of these 12 cases, histopathology of 5 cases was consistent with lepromatous leprosy with high BI (range 1-5), 4 cases were consistent with diagnosis of tuberculoid leprosy and 3 cases were from borderline leprosy spectrum.

Classification

Out of 30 cases, none belonged to TT, 6 belonged to BT, 8 belonged to BB, 9 belonged to BL and 7 cases were classified as LL cases on clinical grounds, Out of 2 cases of neural leprosy, one was classified as BL and the other as BT.

Reactions

A total of 10 (33%) cases presented with features of a reaction, at the time of diagnosis. Out of these, 7 cases had a type 1 (reversal) reaction and 3 had a type 2, erythema nodosum leprosum (ENL) reaction. Among type 1 reaction, 4 cases were BB, 2 BL and 1 BT patient. While 2 out of 3 cases with type 2 reactions were BL and 1 was LL case

Discussion

This study included clinical and epidemiological profile of 30 patients. The most common age group presenting with leprosy was 25-34 years, however, leprosy was detected in as young as 9-year-old boy. Mean age of presentation was 36.47±17.57 years which is younger than reported in other studies. This may be due to better awareness and early detection of leprosy. There was preponderance of male patients with M:F of 3.2:1. This may be due to the fact that males in our community are the major working group and stay more time outdoors than females who mainly remain confined to home and therefore, less likely to get the infection. Another reason might be that females are difficult to screen due to social reasons. However, females presented in younger age group i.e. 15-24 years. These results are consistent with other studies in our part of world. A study from northern regions of Pakistan showed average age of 40 years and male to female ratio was 4:1 which are consistent with our study.[3]

The detection of leprosy in children less than 15 years of age reveals an active circulation of bacillus, continued transmission and lack of disease control by the current health system, as well as, failure of monitoring of the endemic areas.[1]

History of a household contact was given in 11 (37%) cases. In 4 (36%) of these cases, it was a parent and in another 4, a sibling. This higher percentage indicates importance of contact tracing. Several studies indicate that contacts found in other places than the household are also at risk of developing leprosy. The type of leprosy and the bacterial index are the main patient-related factors involved in transmission, but also contacts of PB patients have a higher risk of contracting leprosy as compared to the

general population. The most important contact-related factors are the closeness and intensity of the contact and inherited susceptibility.[4,5] The significance of immunological and molecular markers in relation to risk of transmitting or developing leprosy is not yet fully understood, but there is an indication that contacts that are seropositive for anti-PGL-I antibodies are at increased risk of developing clinical leprosy.[5] The presence of a BCG scar is likely to be related to a lower risk.[6]

Most of the patients were from Sindh and Baluchistan. The cases in Baluchistan were found to be clustered in Makran region. Out of the 5 cases from Baluchistan, 4 belonged to Awaran, a remote area in Makran, indicating the clustering pattern of the disease. All the cases belonged to lower socioeconomic class; the causes may be genetic predisposition, outdoor activities, poor nutritional status and delayed report to healthcare facilities.[7]

The most frequent type of leprosy was BL (30%) followed by BB (27%). BL is highly infectious so these patients may transmit it to their healthy contacts. A higher number of patients at lepromatous pole may indicate lower overall immunity of our population which may be due to malnutrition or genetic factors.[8] Another interesting finding was the abundance of cases diagnosed as BB cases. BB is immunologically most unstable form of leprosy which quickly upgrades or downgrade, so the diagnosis is rare at this stage.[9] The higher number of BB patients in our study, however, warrants early case detection and active screening of disease. The higher proportion of multibacillary cases indicates continuing transmission and the proportion of grade 2 disabilities shows lack of awareness about the early signs and symptoms of the disease, as well as, inability of health services to detect cases early enough.[10] At the genetic level, about 28 genes have been found which are associated with leprosy subtypes or implicated in the polarization process.[11,12] These findings are in contrast to the study by Khan *et al*.[4] from northern areas of Pakistan which indicated frequency of BT as 50% and BL (26%). Another study by Soomro *et al.*[13] from Larkano region of Pakistan also showed BT to be the commonest type of leprosy.

The most frequent presentation was erythematous plaques and patches followed by punched out plaques. Ulnar nerve was the most common nerve enlarged (83%) which is similar to the studies by Soomro *et al.*[13] and Calabar *et al.*[14] It was followed by common peroneal nerve. Among other features, bilateral madarosis and ulcers in hands and feet were common findings. In most cases, ulcers were caused by burn injuries in anesthetic limbs. Nerve pain and paresthesia were reported by 20% of cases. Nasal stuffiness, epistaxis and edema feet were also frequent.

A total of 10 (33%) cases presented with features of a reaction, at the time of diagnosis. Out of these, 7 cases had a type 1 (reversal) reaction and 3 had a type 2, erythema nodosum leprosum (ENL) reaction. Type 1 reaction was seen in 4 cases of BB, 2 BL and 1 BT patient. While 2 out of 3 of patients who presented with Type 2 reactions were BL and 1 LL case, therefore, the BL leprosy is more likely to present with reaction. Lepra reactions are the cause of most of complications and disabilities related to leprosy.[15] Various genetic and immunological factors determine the type of leprae reaction.[16]

The diagnosis and classification of leprosy is mainly clinical, supported by bacillary index and histopathology.[17] Out of 30, histopathology was performed in 12 cases where the differential diagnosis other than leprosy was considered.

To conclude, leprosy is still prevalent in Pakistan and shows clustering in certain geographical areas. Childhood leprosy is also frequent which shows persistent transmission of bacillus. Large scale clinical and epidemiological studies are required to control leprosy in Pakistan. Active case detection and awareness of doctors and community should be done for early diagnosis to prevent disabilities.

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