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Original Article

Clinico-histopathological Concordance in Leprosy Patients - A Study of 200 Cases

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As information about profile of leprosy from different geographical areas is important, this study was carried out to document the clinical profile of leprosy cases reporting to a medical college, a tertiary care settings in Rajkot, Gujarat. Further this study also aimed at analysing the concordance of clinical findings with bacteriological and histopathological characteristics. 200 leprosy patients who came to Dept. of D.V.L., P.D.U. G.M.C, Rajkot from October 2014 to September 2016 were included. Thorough history with routine investigations, slit skin smear, biopsy for H & E and Fite Faraco stain was undertaken. The most common age group was 21-30 years (31%) with male to female ratio 1.82:1. 15 (7.5%) of these cases were migrants. 71.5% were multibacillary patients. 8% were relapse cases. Only 3 (1.5%) belonged to paediatric age group. Clinically maximum patients (91, 45.5%) were of lepromatous leprosy followed by borderline tuberculoid leprosy (46, 23%). An overall 65% of these cases were positive for acid fast bacilli (AFB) in slit skin smears. 17% had Type II reactions whereas only 2% had Type I reactions. 36% of these patients had grade I and 12.5% had grade II deformity. The most common histopathological entity was borderline tuberculoid (25%) followed by lepromatous leprosy (24.5%). Maximum clinical concordance was seen in borderline lepromatous (72.72%. The histopathological diagnosis was consistent with clinical diagnosis in 116 cases (58%) which indicates the need for strengthening of skills and or more research into criteria or dynamics of disease spectrum in this area. A combined approach including clinical, bacteriological and histopathological examination would be desirable to reach at final diagnosis and classification in tertiary care/referral centres. Population based studies followed by intensification of anti-leprosy activities appear to be necessary in this area.

Key words : Leprosy, Histopathology, Epidemiology, Disability, Type I & II reaction, Concordance

Introduction

Leprosy is a chronic spectral granulomatous disease caused by *Mycobacterium leprae* in which the clinical and histopathological features reflect cell mediated immunity status of the host to this organism. World Health Organization (WHO) has defined a case of leprosy as a person having one or more of the following features : hypopigmented or reddish skin lesions with definite loss of sensations; involvement of peripheral nerves (demonstrated by definite thickening with loss of sensations), and skin smear positive for acid fast

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bacilli (Parasad & Kaviasaran 2015). Leprosy can be clinically divided into indeterminate, tuberculoid, lepromatous, borderline group (borderline tuberculoid, midborderline, borderline lepromatous) and rare variants of leprosy (Histoid, pure neuritic, Lucio, Lazarine). It is diagnosed by clinical examination (cutaneous, nerves, sensory and motor examination), bacteriological examination (Bacterial index and morphological index by Ziehl Neelson and Fite Faraco staining method) and histopathological examination (Prasad & Kaviasaran 2015).

As per NLEP report, a total of 125785 new cases were detected in India during the year 2014-15, giving Annual New Case Detection Rate (ANCDR) of 9.73 per 100,000 population (NLEP report 2014-15). As per WHO, India has 60% of the global new leprosy cases (WHO 2015). Need to intensify the activities in different parts of country will be logical strategy in moving towards elimination of disease across entire country and will be dependent upon information about ground realities of leprosy situation. While the cases reporting to a tertiary care settings may or may not reflect true epidemiological picture at field level, the profile points to likely problems about delay, access to services and also needs of strengthening training and management at various levels. As such recent published information is lacking from the Rajkot area, the present study was carried to understand the clinical profile of leprosy patients reporting to our medical college hospital, with a focus on clinicopathological spectrum, bacteriological positivity, reaction and disabilities in these patients. This study has also tried to look into the role of histopathology in the context of its usefulness to cases reporting to a tertiary care centre settings in this area.

Material and Methods

Leprosy patients coming to Department of Dermatology, Venereology and Leprosy of PDU, GMC Rajkot (a Tertiary Care Centre), during a 2 years period from October 2014 to September 2016 were included in this study. It was an observational, cross-sectional study. All patients of leprosy irrespective of age and sex were included except those whose biopsy could not be taken. Relevant data such as age, sex, duration of lesions, course of disease, treatment history, concomitant illnesses, personal habits, family history and past history were collected. All the patients were subjected to thorough clinical, general physical and local examination including cutaneous, nerves, sensory and motor examination (Prasad & Kaviasaran 2015) and examination of eyes, ear, nose, throat and musculoskeletal system. Routine hemogram including complete and differential blood count, erythrocyte sedimentation rate (ESR) was done. Urine routine and microscopic examination and blood biochemistry was performed. G6PD testing was done prior to starting Dapsone. Slit skin smear with Ziehl Neelsen stain for acid fast bacilli. Biopsy for H & E stain and Fite-Faraco stain was done for assessing the clinico-pathological correlation. X rays of the relevant joint and bone was done in patients with deformity. Ophthalmologist's and ENT surgeon's opinion was sought for in all cases. Disabilities were graded according to WHO grading system (Brandsma & van Brakel 2003).

Counselling was done in all patients who were advised regarding hand, foot and eye care. Treatment in the form of MDT MB/PB was started in all the patients as per NLEP treatment guidelines and were kept in regular follow-up. Wherever possible the family members were also screened for leprosy.

Results

Among 200 patients of leprosy studied maximum patients i.e. 62 (31%), were in the age group of 21-30 years. The mean age was 38.5 years with

the youngest patient of 7 years and the oldest of 80 years age. 3 (1.5%) patients were in paediatric age group with age ⩽14 years. Proportion of male patients, 129 (64.5%), was only marginally higher with male to female ratio being 1.82:1. 185 (92.5%) of the patients belonged to various districts of Gujarat. Maximum migrant leprosy patients were from the state of Bihar 7 (3.5%) followed by Madhya Pradesh 4 (2%), Uttar Pradesh 3 (1.5%) and Nepal 1 (0.5%).

The proportion of multibacillary cases, 143 (71.5%), was significantly higher than pauci-bacillary, 57 (28.5%). 16 (8%) patients had a history of contact with a family member suffering from leprosy. 16 (8%) patients were relapse cases who had completed fixed duration MDT therapy in the past. 1 (0.5%) patient had taken dapsone monotherapy and 44 (22%) were treatment defaulters. Maximum, 91 (45.5%), patients were of lepromatous leprosy followed by borderline tuberculoid leprosy 46 (23%), borderline lepromatous leprosy 33 (16.5%), tuberculoid leprosy 24 (12%) and mid-borderline leprosy 6 (3%). Histoid leprosy was diagnosed clinically in 2 (1%) patients while no case of indeterminate leprosy was reported clinically. 34 (17%) had Type II reaction in the form of erythema nodosum leprosum and 2 (1%) patients had Type I reaction. 72 (36%) patients had grade I and 25 (12.5%) had grade II deformity.

AFB positivity was observed in 130 (65%) cases. All cases of lepromatous leprosy and 31 (93.94%) of borderline lepromatous leprosy were AFB positive. All cases of tuberculoid leprosy and 36 (78.26%) cases of borderline tuberculoid group were AFB negative. Among lepromatous leprosy patients, 42 (46.16%) had a BI of 6+ followed by 36 (39.56%) with 5+ and 13 (14.28%) with 4+. Among the borderline lepromatous leprosy, maximum patients 15 (45.45%) had BI of 4+ followed by 10 (30.33%) patients with 3+ and 5 (15.15%) with 5+. Among borderline tuberculoid, 36 (78.26%) patients were AFB negative while 8 (17.39%) cases had BI of 2+ and 2 (4.34%) had BI of 3+ (Table 1).

Table 1: Distribution of patients according to bacteriological index in various types of leprosy in present study

Type of Leprosy	Bacteriological Index							Total no of cases
	0 (%)	1+	2+ (%)	3+ (%)	4+ (%)	5+ (%)	6+ (%)	
TT	24 (100)	-	-	-	-	-	-	24
BT	36 (78.26)	-	8 (17.39)	2 (4.34)	-	-	-	46
BB	1 (16.67)	-	1 (16.67)	2 (33.33)	2 (33.33)	-	-	6
BL	2 (6.07)	-	1 (3.03)	10 (30.3)	15 (45.45)	5 (15.15)	-	33
LL	2 (2.19)	-	-	-	13 (14.28)	36 (39.56)	42 (46.16)	91
Total cases	65 (32.5)	-	10 (5)	14 (7)	30 (15)	41 (20.5)	40 (20)	200

Table 2 : Table showing correlation between histopathological and clinical diagnosis in various types of leprosy included in the present study

Histopathological diagnosis	Clinically diagnosed cases				
	TT (%)	BT (%)	BB (%)	BL (%)	LL (%)
TT	12 (50)	6 (13.04)	-	-	-
BT	6 (25)	31 (67.39)	3 (50)	4 (12.12)	6 (6.59)
BB	-	-	1 (16.66)	-	-
BL	-	3 (6.52)	1 (16.66)	24 (72.72)	17 (18.67)
LL	-	-	-	1 (3.03)	48 (52.74)
IL	6 (25)	5 (10.87)	1 (16.66)	1 (3.03)	-
Type I Reaction	-	1 (2.17)	-	-	-
Type II Reaction	-	-	-	3 (9.09)	20 (21.96)
Total cases	24	46	6	33	91

The most common variant encountered on histopathological examination was borderline tuberculoid leprosy, 50(25%), followed closely by lepromatous leprosy, 49(24.5%), and borderline lepromatous leprosy 45(22.5%). Tuberculoid leprosy was seen in 18 (9%) cases, mid-borderline leprosy in 1 (0.5%) and indeterminate leprosy in 13 (6.5%) cases. 25(12.5%) cases showed type II reaction and 1(0.5%) patient type I reaction. (Table 2) The maximum clinic-pathological concordance, i.e., the cases clinically diagnosed and later histopathologically confirmed, was seen in borderline lepromatous 24 (72.72%), followed closely by borderline tuberculoid 31 (67.39%) and lepromatous leprosy 48 (52.74%). Maximum histopathological concordance was seen in mid-borderline leprosy followed by lepromatous leprosy and tuberculoid leprosy. The histopathological diagnosis was consistent with the clinical diagnosis in 116 cases out of 200, making an overall parity of 58%.

Discussion

Highest point prevalence, 62 (31%), was seen in the age group of 21-30 years which is comparable to findings of Jindal et al (2009) who reported 29.44% patients in this age group. Most of the leprosy patients were in their second or third decade during the time of presentation. Although leprosy may be occurring with equal frequency without any sexual predilection in both males and females, but presentation to the health centre is more in male population. In the present study, we found male preponderance (64.5%) with male to female ratio being 1.82:1 which is lower than ratio of 2.97 reported by Jindal et al (2009) and 2.87 by Tiwary et al (2011). This comparatively higher proportion of female patients may be due to rising female literacy, increased awareness and changing social perceptive towards importance of female health care. 185(92.5%) patients belonged to various districts of Gujarat which was also seen in Jindal et al (2009), where 71.78% patients were from the state where study was conducted. Maximum immigrant leprosy patients were from the state of Bihar 7 (3.5%) which around that time was among one of the 8 states in India having districts with prevalence rate of >2/10,000 population (NLEP 2014-15). Remaining migrants belonged to Madhya Pradesh 4(2%), Uttar Pradesh 3(1.5%) and Nepal 1(0.5%). These

trends are meaningful but need to be confirmed by properly planned epidemiological studies in the population of this area.

The proportion of multibacillary cases 143 (71.5%) was significantly higher than pauci-bacillary patients 57(28.5%). Tiwary et al (2011) reported a lower proportion of multibacillary cases as compared to paucibacillary cases till the year 2005 (average 45% MB against 55% PB), which then suddenly started to rise and reach around 65% MB against 35% PB cases by the end of 2009. The high proportion of multibacillary cases that too with very high BI appears to be sign of existence of inaccessible pockets of population harbouring undiagnosed leprosy patients for a long time (Tiwary et al 2011). Interestingly, the proportion of child cases was very low in our study. It will be worthwhile to investigate whether child cases are being missed, or detected late in this area or rise in bacillated MB cases is recent in this area whose impact will be felt after some time.

In our study, only 16(8%) patients had a history of contact with a family member suffering from leprosy either in past or present although the type of leprosy could not be ascertained in all of them. This was comparable to Jindal et al (2009) where also 9.2% patients had history of contact with a family member with lepromatous leprosy. This may indicate community acquired infections which appear likely by very high proportion of multibacillary bacilliferous leprosy cases in this population.

Adherence to treatment appears to be a problem in this area. In the present study, 16 (8%) had completed fixed duration MDT therapy in the past, 1 (0.5%) patient had taken dapsone monotherapy for 10 years and 44 (22%) were treatment defaulters i.e. they had not completed MDT MB therapy within 18 months or MDT PB therapy within 12 months of initiation of treatment. The remaining 139(69.5%) presented with leprosy for the first time. 16 out of 200 (8%) were relapse cases in our study. Although the treatment papers were not available in most of the patients and the data obtained was based on the history given by the patient or relatives. A reliable determination of relapse rate is the single most important parameter determining the efficacy of MDT (Thappa et al 2016). It has been reported that despite two years of regular therapy, 10% of patients continue to harbour viable persisters (Malathi & Thappa 2013). While no speculation on the effectiveness of current MDT in bacilliferous cases of this area will be proper, the situation demands such studies in this population.

In our study, 72 (36%) patients had grade I deformity/ disability while 25 (12.5%) had grade II deformity/diability. Ulnar claw hand was the most common motor deformity seen. This highlights the importance of improvements in terms of early diagnosis and treatment of leprosy patients including reactions/neuritis as these deformities are the major cause of socioeconomic dehabilitation. This deformity rate is on the higher side (NLEP 2014-15) and may be indicative of late reporting as well as inadequate treatment in some cases.

Maximum, 91 (45.5%) patients were of lepromatous leprosy followed by borderline tuberculoid 46 (23%), borderline lepromatous 33 (16.5%), tuberculoid 24 (12%) and mid-borderline leprosy 6(3%). This was in contrast to Giridhar et al (2012) and Bijjaragi et al (2012) where borderline tuberculoid leprosy was the most common variant with 43.87% and 47.9% of patients respectively while lepromatous leprosy was present in 17.35% and 15.2% of patients respectively. This shows that profiles of disease may vary from area to area and will be indicative of access to services, awareness and manage-

ment practices. Considering these variations, it will be necessary to carry out actual assessment of situation in different areas for devising need based strategies.

Regarding the incidence of reactions, 34 (17%) patients had Type II reaction in the form of erythema nodosum leprosum (ENL) and 2 (1%) had Type I reaction. Jindal et al (2009) also reported similar incidence of Type II reaction with 17.18% cases, however the proportion of Type I Reaction was higher in them being 14.11%. This difference could be due to the relatively lower proportion of borderline tuberculoid cases in the present study. Out of the 34 patients with ENL in present study, 8 (23.53%) presented with erythema nodosum necroticans.

Assessment of bacteriological positivity is very important from the programmatic point of view as this shows the risk of transmission in the community. In the present study, 24 (100%) cases of tuberculoid leprosy and 36 (78.26%) cases of borderline tuberculoid leprosy were AFB negative compared to 100% and 69.05% reported by Giridhar et al (2012). In our study, 91 (100%) cases of lepromatous leprosy and 31(93.94%) cases of borderline lepromatous leprosy were AFB positive in comparison to 100% positive cases in Giridhar et al 2012). The AFB negative cases found in lepromatous spectrum might be due to problems with quality of approach/technique used, also may be due to past treatment and the issue merits to be addressed by proper investigations.

The most common variant encountered on histopathological examination was borderline tuberculoid leprosy 50(25%) followed closely by lepromatous leprosy 49(24.5%), borderline lepromatous leprosy 45(22.5%) and tuberculoid leprosy 18(9%) (Table 2). Giridhar et al (2012) and Bijjaragi et al (2012) also reported borderline tuberculoid leprosy as the most common histopathological types. 1 (0.5%) cases showed midborderline leprosy, 25(12.5%) showed type II reaction and 1(0.5%) type I reaction histopathologically. The higher proportion of type II reaction seen histopathologically could be attributed to higher proportion of clinically diagnosed multibacillary patients with erythema nodosum leprosum in the present study. 13(6.5%) cases showed histopathology of indeterminate leprosy similar to Bijjaragi et al (2012) although there was no case of indeterminate leprosy reported clinically in the current study. This signifies the importance of histopathological examination in such types of leprosy.

Maximum clinic-histopathological concordance, i.e., the cases clinically diagnosed & classified and later histopathologically confirmed, was seen in Borderline lepromatous leprosy 24(72.72%), followed closely by borderline tuberculoid leprosy 31(67.39%) and lepromatous leprosy 48(52.74%) in contrast to Bijarragi et al (2012) where maximum clinical concordance was seen in polar ends of the spectrum, namely lepromatous (76.9%) followed by tuberculoid (75%). Maximum concordance for the histopathological diagnosis was seen in mid-borderline leprosy followed by lepromatous and tuberculoid leprosy. The histopathological diagnosis was consistent with the clinical diagnosis in 116 cases out of 200, making an overall parity of 58% which is comparable to Giridhar et al (60.23%) and Bijjaragi et al (57.3%). Such differences could be attributed to the stringency of criteria used, clinical spectrum of cases studied and relative number of cases of each type of leprosy in various studies. It will be important to resolve these issues and upgrade the skills for optimum management of cases.

The disparity between clinical and histopathological observations was anticipated because the parameters used for the histopathologic

classification are well-defined, precise and also take into account the immunologic response of the tissue, while the clinical classification gives recognition only to the gross appearances of the lesions which is due to the underlying pathological change. Both clinical and histopathological diagnosis can be very challenging in cases of leprosy. Moreover few leprosy cases, mainly those in borderline group, are in a continuously changing immunological spectrum, histolopathological classification in such circumstances possibly gives a better and earlier indication for any recent shift in the spectrum. The bacterial index gives an idea about the burden of the infectious disease cases in the community and also helps in monitoring the response to treatment. Histopathological examination would also help in identifying an early reaction not evident clinically as well as in confirming diagnosis of clinically doubtful cases of leprosy. It would be particularly important in cases of indeterminate leprosy. The incorporation of these three parameters would be important to arrive at more accurate diagnosis & classification based on immunological spectrum of patient and better assessment of load of infectious cases. Hence a combined approach including clinical, bacteriological and histopathological examination will be desirable at tertiary care settings for all the leprosy patients.

To conclude, profile of leprosy reporting to our Tertiary care centre suggests late reporting of patients in this area, cases are possibly being diagnosed when many of them have already progressed to bacilliferous stages and many afflicted with disabilities which could have been prevented. There is clear need to carry out field studies in this area and then intensify the programme accordingly.

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