CLINICAL PROFILE OF HANSEN'S DISEASE PATIENTS IN THE MULTIDRUG THERAPY ERA AT THE UNTH, ENUGU

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SUMMARY

Background: Leprosy continues to be one of the major public health problems in many countries including Nigeria. It is an infectious disease caused by *Mycobacterium Leprae*. After the commencement of the multi drug therapy (MDT) era and its accompanying anti-leprosy measures in Nigeria [through the National TB and Leprosy Control Programme (NTBLCP)], leprosy patients attending the Skin clinic of University of Nigeria Teaching hospital, Enugu, were assessed over a five year period (1997-2001).

Objective: The aim of the study was to document the current profile of Hansen's disease in a tertiary hospital setting in this MDT era.

Results: Four hundred and nineteen patients had leprosy and 271(64.7%) benefited from MDT: 21(5.1%) were children and 390 (94.8%) adults. The patients were aged between 5-81 years, with a female preponderance of 248 (60.3%). Main findings were prevalence of 3.9% for leprosy with new case detection rate ranging from 0.4 in 1997 to 0.73 in 2001.

New cases presented more regularly to the skin clinic since 2000 ($p<0.05$). Observed clinical patterns were paucibacillary leprosy 61.3% and multibacillary leprosy 38.7%. Solitary skin lesions were seen in 21.4%, primary neurotic leprosy in 8.3%, atypical forms (such as vitiligo in leprosy) in 17.1%, reactions in13.7%, leprosy in association with AIDs in 5.6%, disabilities in 19.1% and relapses in 3.8% of the cases. Distribution of vitiligo were multiple, extensive and occurred at sites entirely different from its occurrence in patients without leprosy.

Conclusion: Although the NTBL control generated a lot of awareness and positive impact on leprosy control within communities around Enugu, early diagnosis of leprosy is still problematic. The spectrum of the disease is still wide in Nigeria.

Key Words: *Leprosy, clinical profile, MDT (Multi Drug Therapy) Era, Nigeria*

INTRODUCTION:

Leprosy is a chronic communicable disease caused by *Mycobacterium leprae* which attacks mainly the peripheral nerves, the skin and the mucosa of the upper respiratory tract. It is a disease of antiquity that is still worldwide but most prevalent in Asia, Africa, South and Central America [1-3]. In Nigeria it has been a major public health problem particularly in the North and parts of the south where it has been associated with a lot of myth[4].

It was believed to be a punishment from God, as well as being a hereditary disease. In addition because the patients suffered physical deformities, the disease was associated with great fear and social stigma. Patients were therefore ostracized from their families. Consequently in the past, missionaries and voluntary agencies built settlements (leprosariums) to serve as a place of solace for sufferers. The nearest such settlements to Enugu was at Oji River and this was built in 1932[4].

Leprosy control was with dapsone monotherapy for well over 30years until the emergence of dapsone resistant strains of M. leprae jeopardized this[2,3]. Dapsone

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Accepted for Publication: 8th July 2003

monotherapy, used since 1940, required more than 5 years of regular treatment to render most, but not all, the lepromatous [multibacillary (MB)] patients eligible for discharge. This is unlike the multi drug therapy (MDT) that was effective in a relatively short time. The leprosy unit of the World Health Organization (WHO) in October 1981 took the initiative of convening a Study Group on the "Chemotherapy of Leprosy for Control Programs," having documented evidence on the efficacy of MDT (Multi Drug Therapy) in humans and recommended a combination of three drugs – rifampicin, dapsone and clofazamine. The multibacillary (MB) regimen consisted of supervised monthly rifampicin and clofazamine and daily clofazamine and dapsone. Recommendations for paucibacillary (PB) patients were supervised monthly rifampicin plus unsupervised daily dapsone. These recommendations received their ultimate endorsement from the WHO sixth expert Committee in 1987 in the following words: "In view of the very favourable results so far, the Committee strongly endorses the continued use of the standard MDT regimens." Concurrently, the Medical Commission of the International Federation of Anti-leprosy Associations, ILEP, also embraced the WHO recommendation, thereby enabling the activities of 22 NGOs in 16 countries, supporting leprosy control in 104 endemic countries to carry out the WHO/ MDT recommended protocols. The implementation of MDT underwent several modifications over the years in which it has been at the core of the Leprosy Elimination Program.

Multi Drug Therapy (MDT) is a major advance in leprosy control and early treatment with MDT will kill the bacilli and cure the patient entirely before any damage to hands, feet or other disfiguring features occur. The cured person may then return to a normal life and not be seen as a cured leper. So far, the WHO had made commendable progress towards the 'elimination of leprosy' with MDT. It is hoped that the days of leprosy as a disfiguring disease may soon end. Staff working in the field advocate that leprosy should now be regarded as nothing but a "treatable skin disease"[1].

The National Tuberculosis and Leprosy Control Programme (NTBLCP) was established in 1989 and it adopted the WHO recommended Multi-Drug Therapy (MDT) strategy for the control of leprosy within an integrated Primary Health care system in Nigeria. Nigeria made significant progress in leprosy control with substantial technical and financial support from WHO and member associations of the International Federation of Anti-leprosy Association. The disease burden has reduced from 250,000 in 1989 to 7000 in 1999 giving the current prevalence of 0.6 per 10,000 population[5].

Despite all these, case detection for Hansen's disease is still problematic within Nigeria, as well as getting cured patients reabsorbed into their communities. The social stigma and discrimination still exist, especially for leprosy patients with physical deformities and disabilities. In view of the recently reported prevalence values, the gains and successes of MDT in Nigeria, one is tempted to ask if this is a reflection of an actual reduction in the transmission of leprosy infection around Enugu or whether there are still pockets of reservoirs that have not been reached.

Consequently, the profile of patients with leprosy seen at the Skin clinic of the UNTH, Enugu was analyzed.

MATERIALS AND METHOD:

A retrospective study of leprosy patients seen in the skin clinic of the University of Nigeria Teaching Hospital, Enugu, between 1997 and 2001 was done. Thirteen of them were also studied prospectively.

All the patients were registered and followed up under the National Tuberculosis and Leprosy Control Programme (NTBLCP). The case notes, NTBLCP record cards and treatment records were reviewed. The relevant demographic and clinical data, duration of disorder, results of bacterial studies, report of histological examination of biopsies and or skin smears, records of complications and disabilities were extracted and analyzed. Slit skin smears were taken routinely in all suspect cases, while biopsies were carried out on highly suspicious cases after the patient had given an informed

consent. The skin biopsies done for standard pathologic examination and the Fite-Farraco staining were required for confirmation of diagnosis in suspicious and or atypical cases.

A diagnosis of leprosy was made if a person with suspect skin lesions was found to have loss of sensation in a skin lesion or an enlarged peripheral nerve trunk or a positive slit skin smear. The bacterial study was judged positive if in 100 oil immersion fields there were one or more *mycobacterium leprae* bacilli and the bacterial index (BI) was1+ or greater on the Ridley scale[6-8].

All patients with a positive smear were termed multibacillary (MB).Those with negative skin smears were termed as paucibacillary (PB). All paucibacillary leprosy patients who had received treatment for 6-12 months and multibacillary patients who had either received treatment for 24 months or until they became smear negative were evaluated. This was taken as the end point in accordance to the standard MDT treatment protocol that had been adopted for this study.

The prevalence and new case detection rates were also calculated. Results were analyzed using the one way analysis of variance (ANOVA); student t test, standard normal distribution (SND) or Z-score for comparison of means and chi squares(X^2) for comparison of proportions. The differences were considered statistically significant if P-value was <0.05. Statistical analysis was done using the SPSS software.

RESULTS:

Table 1: Age and Sex Demography of 411 Leprosy Patients

Age	Male	female	Total	%
0 – 16	10	11	21	5.1
17 – 32	57	83	140	34.1
33 – 48	45	61	106	25.8
49 – 64	27	47	74	18.0
65 – 80	19	39	58	14.1
≥ 81	5	7	12	2.9
Total	163	248	411	100.0

During the 5 year study period, 419 patients had leprosy and 271(64.7%) benefited from MDT. Four hundred and eleven folders were identified and used for the analysis. Table 1 shows the demographic data of these patients. Leprosy affected 21(5.1%) children and 390 (94.8%) adults aged between 5-81 years, with a marked female preponderance 248 (60.3%). The sex ratio was 1: 1.5. The mean age at detection was 41.7±15.3 years and the number of children with Hansen's disease peaked at 10 years of age. The earliest recorded onset of symptoms occurred in two patients at the age of 4years.

Table 2: Duration of rash/disorder

Duration of rash (years)	No of patients	(%)
0-5	57	13.9
6-11	154	37.4
12-17	66	16.1
18- 23	9	2.3
≥24	4	0.9
Unsure	121	29.4
Total	411	100.0

The duration of the illness was particularly more prolonged amongst adults than children ($p<0.05$). That is the duration from the time the patient could recall the onset of his symptoms to the time when the diagnosis was confirmed exceeded 11 years in 211(51.3%) while 121 (29.4%) were unsure of the onset and duration of illness (table 2). The latter group had the greatest impairments observed. There was positive history of contact in 63 (15.3%) of cases.

Table 3: Mucocutaneous Manifestations of Hansen's disease in Enugu, Nigeria

SKIN MANIFESTATION*	No	%
Nodular/micropapular eruptions	91	22.1
Solitary Hypopigmented Macules	66	16.1
Disabilities	59	14.4
Plaques and Nodular Eruptions	57	13.9
Atypical Forms**	53	17.1
Reactions (ENL, Reversals)	42	10.2
Multiple Irregular Plaques/Macules	39	9.5
Collapse of Nasal Bridge	33	8.1
Conjunctivitis	20	4.9
Epistaxis	17	4.1
Primary Neuritic Leprosy	14	3.4
Ichthyosis	7	1.7
Onchocerciasis	3	0.7
Others (Leprosy and HIV)	9	2.2

*Some patients had multiple more than one manifestation
**Depigmentations (vitiligo), Swollen Faces and Limbs

The prevalence of leprosy at our Skin clinic over the study period was 3.9% with new case detection rate ranging from 0.4 in 1997 to 0.73 in 2001[2]. New cases had presented more regularly at the Skin clinic since 2000 ($p<0.05$). Manifestations of the disease varied from case to case (table 3). Paucibacillary leprosy constituted 252 (61.3%) of the cases and were mostly females while multibacillary leprosy accounted for 159 (38.7%). The rash was widespread with multiple non-scaly papules and nodules at initial presentation in 196 (47.7%). This was the commonest presentation amongst multibacillary individuals. The papules, mainly in clusters were found on the extremities, ear lobules and face (fig. I) alongside areas of either hypoesthesia or dysaesthesia. Amongst the atypical cases (17.1%) were those with extensive vitiligo. The depigmented areas had no epidermal surface changes, were symmetrical and involved the shoulders, trunk, breasts, buttocks and thighs (figure 2).

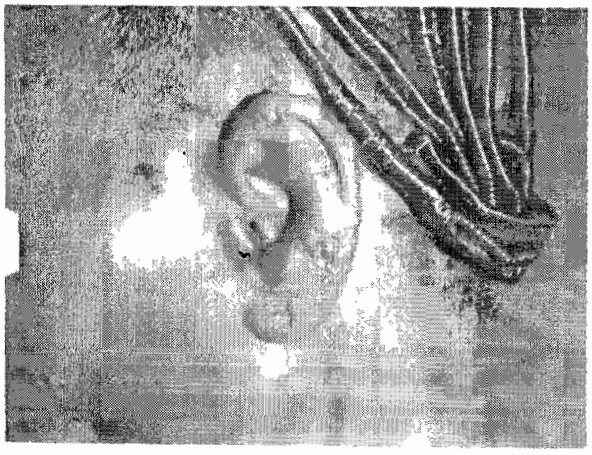

Fig. 1: Papules in clusters on the face earlobes and back

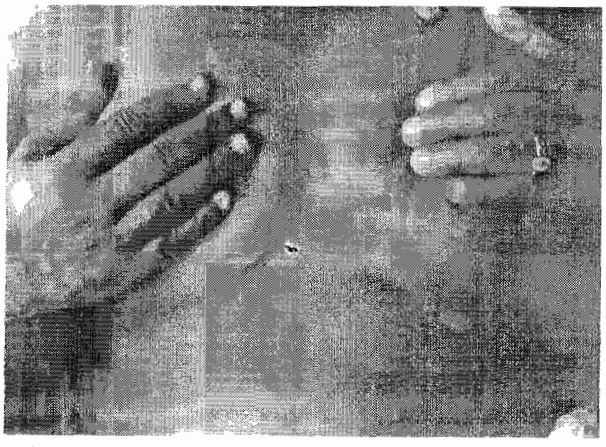

Fig. 2: Vitiliganous macules on trunks and limbs

Multibacillary individuals had the most deformities and also had severe reactions to the antileprae drugs. There were 18 individuals (4.3%) in this category. Primary neuritic leprosy was not common. It affected 14 (3.5%) individuals whose main symptoms included tingling sensation, intermittent pain, heaviness and swelling of the digits. Only 2.1% of these had associated cutaneous changes around the affected thickened nerves.

Leprosy patients are exposed to other diseases as the general public, hence there were 9 (2.2%) leprosy patients that were HIV positive, 5 (1.2%) had scabies and 3 (0.7%) had onchocerciasis. Deformities observed included collapse of the bridge of the nose(10 .6%), trophic ulcers (2.1%), resorption of the digits (3.9%), muscle wasting(7.7%), claw hand (1.3%), foot drop(8.9%), oedema of the extremities(14.9%), nail changes(2.7%), erythema nodosum leprae reactions, ENL, (5.3%), ichtyosis (4.7%), ectropion and lagophthalmos (3.8%), punctate keratitis (2.2%) and blindness (3.7%).

Treatment modalities employed prior to presentation by the patients, orthodox and traditional medical practitioners varied extensively. Griseofulvin, topical steroids of varied potency and antifungals were the commonest drugs prescribed.

Records also showed that by six months of treatment on MDT, the paucibacillary individuals had made more recovery than the multibacillary group ($p<0.05$), while 31.4% ± 17.7 of the multibacillary individuals were discharged by 24 months. Within the study period 57.8% of all the patients were cured and discharged, 11.3% relapsed and 21.5% defaulted from treatment while lesions were unchanged in 6.4 % of the patients. There were varied reasons for defaulting, majority of which were lack of funds for transportation to hospital and bereavements.

DISCUSSION:

In Nigeria, Hansen's disease is endemic in the Northern part and in a few pockets in the Southern part [4]. Treatment is often delayed due to failure of Medical officers to accurately make the diagnosis. The major risk factors for the

transmission of the disease include family members of patients with the disease, residence or birth in an endemic area, children (in or out of school) in endemic or hypoendemic area and exposure to nine banded armadillos or mangabey monkeys Even though the actual mode of transmission is still not fully understood it is believed that the most likely mode of transmission is by spread of droplets from nasal mucosa of patients with multibacillary disease, particularly in overcrowded areas[7, 8]. A history of contact with infected person was positive in 63 (15.3%) of our cases. These patients were living with at least one family member who had lepromatous leprosy.

Although, MDT has made great impact in the treatment of leprosy in Nigeria and our skin clinic treats leprosy patients in the general clinical service setting so as to eliminate the stigmatization associated with special leprosy clinics, there are still delays in presentation to our Skin Clinic. One hundred and forty three (34.7%) patients had their illness for over 13 years before presenting to the clinic. A clear identification of the point of onset (i.e. exposure and infection) was difficult for adult patients, children and their relatives alike. A few felt their rash was normal, because they recall one or two family members or other close relations with similar rash on their bodies and who had no form of treatment for it. Impairment was also observed to be higher amongst patients that had a longer duration of their disease before presentation. Chen et al[9] in a national survey in China over 14 year-period assessed delays in case detection and patient presentation and related it to clinical and operational parameters on ground since the commencement of MDT in China in the mid-1980s. They identified a median delay period between the patients' observation of the first signs of the disease and confirmation of diagnosis of up to 22 months (24 and 19 months for Multibacillary and Paucibacillary patients respectively). They also observed that age, occupation, nationality, leprosy type and detection methods all affected the delay. Furthermore, individuals with the longest delays had the most impairment. Similarly, our study shows that delays in detection and age are the main risk factors for patients presenting with impairment and deformities.

The prevalence of leprosy at our Skin clinic over the study period was 3.9% with new case detection rate ranging from 0.4 in 1997 to 0.73 in 2001.This was high probably because it was a clinic based study. However, newer cases presents more frequently at the Skin clinic since 2000 ($p<0.0001$) when compared to 1997.

The clinical profile of leprosy is determined by the cellular immune response to *Mycobacterium Leprae* and so has resulted in a spectrum of various clinical forms[2, 6, 10]. At one pole of the spectrum lies tuberculoid leprosy (TT) while at the other extreme lies lepromatous leprosy (LL). Between these two polar types, various borderline forms exists such as borderline tuberculoid (BT), mid-borderline (BB) and borderline leprosy (BL). In tuberculoid leprosy there is localized skin and nerve lesion(s), with a low bacterial load and strong cell mediated immunity. In contrast, lepromatous leprosy has generalized lesions with a high bacterial load and strong humoral immunity. Patients seen at our skin clinic presented with a wide range of mucocutaneous lesions determined solely by their host immunity and reflected all the clinical spectrum of Hansen's disease. Micropapules and nodular forms were the commonest (table 2 and fig. I). Those with micropapules/nodules were mainly multibacillary as there were detectable bacilli on the tissue smears. Males mostly presented with an atypical arrangement of tiny clusters and crops of papules on the extremities and face, often associated with oedema of the underlying skin. We also noticed more paucibacillary leprosy as opposed to reports from the Western part of Nigeria[11, 12]. This could be attributable to the impact of the ongoing leprosy awareness campaign which has probably generated a desire to seek medical care early.

Vitiligo occurred mainly amongst lepromatous leprosy patients. None of the tuberculoid leprosy patients had vitiligo. Vitiligo should be differentiated from the hypopigmented macules of tuberculoid leprosy, which has epidermal changes. Leprosy and vitiligo are known to induce pigment loss, via

different mechanisms[13]. Loss of nervous control of melanogenesis could be one of the mechanisms due to nervous damage in leprosy, while the reasons are unknown in vitiligo[13, 14]. However autoimmune disorders have been described in both diseases.

Indeterminate disease was described in those individuals with solitary hypopigmented macules, which had indistinct borders and no altered sensation. This represents an early stage of leprosy and may progress into any of the forms of the disease. It occurred in 21.4% of our patients.

Primary neuritic leprosy (PNL) was not a common presentation in our patients, but occurred as peripheral neuropathy without present or past evidence of skin lesions of Hansen's disease. Skin biopsy changes showed typical leprosy in cutaneous and subcutaneous nerves.

ENL (Erythema Nodosum Leprae) reactions occurred in 5.3 % of our patients and presented with pain and swelling of the limbs associated with painful crops of tender nodules.

ENL is an immune complex reaction that occurs in patients with multibacillary leprosy and presents with acute inflammation of any tissue harbouring *M. Leprae*[15, 16], while the reversal reaction occurs in all forms of borderline leprosy (BT, BB, BL).

The stigma of leprosy is still prevalent in the South Eastern part of Nigeria, but not as much as it used to be in the pre-MDT era. Once discharged as cured, individuals with minimal disabilities were reabsorbed into the society with less degree of stigmatization.

CONCLUSION

The diagnosis of early (paucibacillary) leprosy continues to be a problem for clinicians, histopathologists and community health extension workers in Nigeria. Findings from this study revealed that the clinical spectrum of leprosy is wider than acceptable in this MDT era for Nigeria. Although vitiligo was seen amongst a significant number of our lepromatous patients its distribution was multiple, extensive and occurred at sites different from its site of occurrence in patients without leprosy.

ACKNOWLEDGMENT

I wish to express my heartfelt appreciation to Dr SMO Nnoruka and Prof. A Ezeoke for their constructive criticisms.

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