Thyroid functional status in leprosy patients in Sudan

M.M. Kheir,[1] A.M. Ahmed[2] and A.A. Elsarrag[3]

حالة الوظائف الدرقية في مرضى الجذام بالسودان

موسى محمد خير وعوض محمد أحمد وعائدة عبد الله السراج

خلاصة: درسنا حالات 45 مصاباً بالغاً بالجذام التورُّمي والجذام الحدي، ممن راجعوا عيادات الجذام بالخرطوم وأم درمان، و لم يسبق أن تلقوا أي علاج، وذلك لتقييم الآثار السريرية والكيميائية الحيوية للمرض في وظائف الدرقية. وأدخلنا في الدراسة مجموعة شاهدة مكونة من ثلاثين شخصاً مماثلين، ليست بهم علامات أو أعراض لأي مرض درقي وذلك لغرض المقارنة. وكانت مستويات الثيروكسين وثالث يود الثيرونين والثيروتروفين في حدود المستويات العادية. أما متوسط مستوى الثيروكسين بالمصل فكان منخفضاً في كلتا المجموعتين (بدرجة يعتد بها في مرضى الجذام التورُّمي وحدهم). أما متوسط مستوى ثالث يود الثيرونين فكان مرتفعاً في كلتا المجموعتين (من دون مغزى إحصائي في أي منهما). وكان متوسط مستوى الثيروتروفين أعلى بدرجة يعتد بها إحصائياً في كلتا المجموعتين بالمقارنة مع الحالات الشاهدة.

ABSTRACT We studied 45 adult patients with untreated lepromatous leprosy and borderline leprosy, presenting at clinics in Khartoum and Omdurman, to assess clinical and biochemical effects of the disease on thyroid function. A matching control group of 30 subjects, without symptoms or signs of thyroid disease, were included for comparison. Thyroxine, triiodothyronine and thyrotrophin levels were within normal range. Mean serum thyroxine was low in both groups (significant in lepromatous leprosy patients only). Mean serum triiodothyronine was high in both groups (significant in neither group). Mean thyrotrophin was significantly higher in both groups compared with controls.

Etat fonctionnel de la thyroïde chez des patients lépreux au Soudan

RESUME Nous avons étudié 45 patients adultes atteints de lèpre lépromateuse et de lèpre borderline non traitée qui se sont présentés dans des dispensaires de Khartoum et d'Omdurman afin d'évaluer les effets cliniques et biochimiques de la maladie sur la fonction thyroïde. Un groupe témoin appareillé comprenant 30 sujets, ne présentant pas de symptômes ni de signes de maladie thyroïdienne, a été inclus pour la comparaison. Les taux de thyroxine, de triiodothyronine et de thyrotrophine se situaient dans la normale. La thyroxine sérique moyenne était faible dans les deux groupes (significatif chez les patients atteints de lèpre lépromateuse seulement). La triiodothyronine sérique moyenne était forte dans les deux groupes (significatif dans aucun des deux groupes). La thyrotrophine moyenne était significativement plus élevée dans les deux groupes par comparaison avec les témoins.

[1]*Department of Medicine, University of Khartoum, Khartoum, Sudan.*
[2]*Department of Medicine, University of Bahr Elgazal, Khartoum, Sudan.*
[3]*Ministry of Health, Khartoum, Sudan.*
Received: 20/02/00; accepted: 02/07/00

Introduction

Leprosy, a chronic infectious disease caused by *Mycobacterium leprae* (an acid, alcohol-fast bacillus), is essentially a disease of peripheral nerves that can also affect the skin and sometimes other tissues, notably the eyes, mucosa of the upper respiratory tract, muscles, bones and testes [*1*].

Very little has been written about the endocrine changes in leprosy. The testes are the most commonly affected endocrine organs. Leprosy may lead to azospermia, sterility and gynaecomastia [*2*]. Kannan found a significant increase in gonadotrophins, while the testosterone level was significantly low [*3*]. Rea obtained similar results regarding the levels of luteinizing hormone (LH), follicle stimulating hormone (FSH) and testosterone [*4*]. Glucose tolerance has been found to be normal in patients with short disease duration, whereas diabetic curves were more common in those with disease duration of more than 2 years [*5*]. Regarding the thyroid functional status in leprosy, Garg et al. studied 43 patients with leprosy and found that protein-bound iodine was normal in all types of leprosy, while mean triiodothyronine (T_3) and thyroxine (T_4) levels were low [*6*]. Balybin obtained different results, with serum T_3 being significantly elevated in his patients [*7*].

In Sudan, leprosy is an important endemic disease affecting a significant proportion of the population, and it is distributed countrywide. Two clinical forms of leprosy, lepromatous leprosy (LL) and borderline leprosy (BL), are particularly important. LL is defined as having more than five skin lesions, distributed more symmetrically, with loss of sensation and many nerve trunks affected. Cases are strongly positive in bacteriological examination [*8*]. In BL, there are 2–5 skin lesions, asymmetrically distributed, with loss of sensation and involvement of only one nerve trunk. Skin smears may be negative, except at lesions [*8*].

Since leprosy is endemic in Sudan, it is important to address unusual manifestations of this disease, such as thyroid dysfunction. The aim of our study was to assess the effects of leprosy on thyroid functional status, both clinically and biochemically, in a group of Sudanese patients.

Methods

The study was conducted in leprosy clinics in Khartoum and Omdurman, Sudan in 1998 and involved 45 patients (35 LL and 10 BL cases). The patients were newly diagnosed and untreated and were not known to have any endocrine disorders or to be on any medication. Males accounted for 68.9% (n = 31) of the total and females 31.1% (n = 14). Age range was 18–62 years, with a mean of 38 years. Sex distribution of the LL group was 24 (68.6%) male and 11 (31.4%) female (mean age: 36 years). In the BL group, 7 (70.0%) were male and 3 (30.0%) female (mean age: 40 years). For the LL group, duration of disease ranged from 1 to 12 years (mean duration: 4.8 years) and for the BL group, duration ranged from 1 to 5 years (mean duration: 2.9 years). No patient reported a history of regular smoking. All patients gave verbal consent to participate in the study.

Diagnosis of leprosy was confirmed by bacteriological examination. Skin slit smears were taken from suspected lesions and sites of predilection. The bacterial load was determined microscopically. Indices ranged between 1^+ and 6^+ in the LL group

(mean: 3.4+), and between 0 and 1+ in the BL group.

Body mass index (BMI) was calculated as: weight (kg)/height^2 (m^2). Categories used were normal (19–24 kg/m^2), overweight (> 24 kg/m^2) and underweight (< 19 kg/m^2). All patients were within the normal range.

A control group, made up of 30 adults recruited from staff at Omdurman Hospital and not known to have any endocrine disorder or to be on any medication, were matched for sex and age to the study group. Of the controls, 20 (70.0%) were male and 10 (30.0%) female (age range: 20 61 years; mean: 37 years).

History, physical examination and laboratory investigation for thyroid dysfunction were performed, taking into consideration the difference between primary and secondary hypothyroidism due to hypothalamic or pituitary disease. Assay for T_3, T_4 and thyrotrophin (TSH) for the patients was performed using radioimmunoassay techniques, and compared to sera obtained from the healthy controls [*9*]. The reference ranges were taken as T_4: 52–154 nmol/L; T_3: 1.08–2.92 nmol/L; and TSH: 0.5–3.5 mU/L. The hormone levels were compared in the two groups separately against the levels of the controls. Results were expressed as mean ± standard deviation. Comparison between sets of data were made using Student *t*-test, with $P < 0.05$ the test for significance.

Results

No symptoms or signs of thyroid disease were encountered. The mean of T_4 value was lower in the LL group compared to controls (Table 1). All T_3 levels in the different groups were within normal ranges and there was no significant difference between the groups. The levels of serum TSH were within normal range, but the mean level was significantly increased in both the BL and LL groups compared to the mean level of the control group (Table 2).

Table 1 Serum thyroxine levels in patients with leprosy compared to controls, Sudan, 1998

Group	Number	Thyroxine Mean ± *s* (nmol/L)
LL leprosy	35	92.91 ± 20.84
BL leprosy	10	107.9 ± 25.57
Control	30	98.50 ± 25.57

LL vs BL: t = *1.908*, P > *0.05 (not significant).*
LL vs controls: t = *0.971*, P > *0.05 (not significant).*
BL vs controls: t = *1.001*, P > *0.05 (not significant).*
LL = lepromatous leprosy.
BL = borderline leprosy.
s = *standard deviation.*

Table 2 Serum thyrotrophin levels in groups with leprosy compared to controls, Sudan, 1998

Group	Number	Thyrotrophin Mean ± *s* (mU/L)
LL leprosy	35	2.59 ± 1.65
BL leprosy	10	3.48 ± 1.80
Control	30	1.63 ± 1.10

LL vs BL: t = *1.475*, P > *0.05 (not significant).*
LL vs controls: t = *2.026*, P < *0.01 (significant).*
BL vs controls: t = *3.896*, P < *0.01 (significant).*
LL = lepromatous leprosy.
BL = borderline leprosy.
s = *standard deviation.*

Discussion

Leprosy is a common disease in Sudan, affecting people of low socioeconomic status, often living in areas far from medical services. This was reflected in the duration

and severity of the disease on first presentation. No specific clinical features of thyroid disease were encountered in this study. Signs and symptoms of peripheral neuropathy were encountered in 32 patients (71.1%). Hoarseness of voice in two patients (4.4%) can be attributed to leprosy itself, as there were no other features specific for hypothyroidism.

The results for serum T_4 and its mean accord with the results obtained by Garg et al. [*6*]. The decrease in the mean value of serum T_4 in LL patients correlates with disease severity, duration and bacterial load. In contrast, Balybin found no difference in serum T_4 concentrations in his leprosy patients compared to controls [*7*]. We found there was a small increase in mean serum T_3 levels in both leprosy groups studied compared to the control group, although this elevation was not statistically significant. Balybin obtained a similar elevated mean serum T_3 result in leprosy patients compared to controls, but the elevation was not statistically significant in LL patients [*7*]. In contrast, Garg et al. found mean serum T_3 to be low in all types of leprosy [*6*]. These opposing results may be due to differences in the duration of the disease in the study samples or in the measurement techniques used. The mean levels of serum TSH were also elevated in both patient groups (LL and BL) compared with controls, and the elevation was statistically significant. Similar results were obtained by Balybin [*7*].

Although we did not carry out histological studies on the thyroid glands of our patients, it does seem that leprosy can affect the thyroid either directly or through an immunological process. Balybin found that endogenous thyroid hormones have immunomodulatory activity closely related to disease activity [*10*]. Our findings suggest that these patients may have suffered from subclinical primary hypothyroidism possibly through a leprosy-triggered silent autoimmune thyroiditis. To consider this possibility, we suggest a prospective study to detect the serum anti-thyroid antibodies in such patients.

Another possibility is that the problem could be one of the variants of sick thyroid syndrome in which the abnormalities in the thyroid functions are actually due to the chronic illness *per se*. It is known that age, sex, BMI, smoking and chronic illness *per se* can affect thyroid function. Our patients were within the normal BMI range and none was a regular smoker. Sex distribution was similar in all groups and our study comprised both young and old patients. A further study among leprosy patients controlled with other chronic diseases, such as tuberculosis, may define a specific role for leprosy in thyroid functional disturbances.

Attention, from time to time, to unusual manifestations of our endemic diseases may lead to interesting findings. We hope that the results of our research will stimulate further investigation of thyroid dysfunction in leprosy patients, using more advanced investigatory techniques and a larger study population.

Acknowledgement

We are deeply grateful for the very valuable help of the late Dr Khalafalla Mohamed Ahmed in initiating this work. Dr Khalafalla was a pioneer of research. He organized the care of leprosy patients in Sudan, and undertook research in addition to his teaching duties in internal medicine at the Faculty of Medicine, University of Khartoum.

References

1. Bryceson A, Pfaltzgraff RE. *Leprosy*, 3rd ed. Edinburgh, Churchill Livingstone, 1990.
2. Grabstald H, Swa LL. Genitourinary lesions in leprosy with special reference to the problem of atrophy of the testes. *Journal of the American Medical Association*, 1952, 149:1287–91.
3. Kannan V, Vijaya G. Endocrine testicular functions in leprosy. *Hormone and metabolic research*, 1984, 16:146–50.
4. Rea. TH. A comparative study of testicular involvement in lepromatous and borderline lepromatous liprosy. *International journal of leprosy and other mycobacterial diseases: official organ of the International Leprosy Association*, 1988, 56:383–8.
5. Garg. R et al. Glucose tolerance test in leprosy. *Indian journal of leprosy*, 1990, 62:50–4.
6. Garg R et al. Thyroid function in leprosy. *Indian journal of leprosy*, 1990, 62:215–8.
7. Balybin ES. Tireoidnye gormony u bol'nykh leproi. [Thyroid hormones in leprosy patients.] *Vestnik dermatologii i venerologii*, 1988, 8:48–51.
8. Ridley DS, Jopling WH. A classification of leprosy for research purposes. *Leprosy review*, 1962, 33:119–28.
9. Kendall-Taylor P. Investigation of thyrotoxicosis. *Clinical endocrinology*, 1995, 42:309–13.
10. Balybin ES. Immunomoduliatornaia rol' endogennykh tireoidnykh gormonov pri mikobakteriozakh. [Immunomo-dulating role of endogenous thyroid hormones in mycobacterioses.] *Problemy tuberkuleza*, 1995, 2:37–9.