Original Article

A Pilot Study on Hypogonadism in Male Leprosy Patients in Rural Tertiary Care Hospital in Central India

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Abstract

Background: Leprosy is a chronic granulomatous infectious disease caused by *Mycobacterium leprae*. Besides the skin and peripheral nerves, it also involves many internal organs. Testicular involvement is mainly seen in leprosy. Hypogonadism in males with leprosy can occur due the involvement of testis. **Aim:** The aim was to evaluate the gonadal function impairment in males with leprosy and to analyze the relation of follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone to the activity, duration, and disease classification in Central India. **Patients and Methods:** This was a prospective observational pilot study. We evaluated 30 patients of leprosy. They were subjected to careful history taking, dermatological and genital examination, assessment of FSH, LH, and testosterone levels, and slit skin smear for acid-fast bacilli. Diagnosis of leprosy was confirmed histopathologically. The collected data were encoded and entered electronically in a computer excel worksheet 2010 version. The statistical analysis was performed using SPSS version 17.0 for Windows. Pearson correlation coefficient was used to establish relationship between different variables. $P \leq 0.05$ was considered statistically significant. **Results:** A positive correlation was found between FSH and LH hormones which was highly significant, whereas there was a negative correlation between testosterone and FSH and LH levels. There was a positive correlation between age, duration of disease, and reaction in leprosy with those of FSH and LH levels. There was a positive correlation between disease activity bacillary index (BI) and FSH, LH and a negative correlation between BI and testosterone. **Conclusion:** It is recommended that lepromatous leprosy patients should be routinely screened for hypogonadism using FSH, LH, and testosterone levels.

Keywords: Hypogonadism, leprosy, testicular dysfunction

Introduction

Leprosy is a chronic multisystem granulomatous disease. The testis is commonly affected by leprosy, resulting in sexual dysfunction and testicular atrophy.[1] Hypogonadism in male leprosy patients is often silent, unreported, and under-estimated.[2] This involves various factors involving alteration in the immune response of the leprosy patient, direct tissue infiltration by leprosy bacilli, and recurrent erythema nodosum leprosum.[3]

The testes are the favored site for *Mycobacterium leprae* due to the lower temperature in the scrotum. They invade the testis through direct invasion through adjacent skin tissue or by lymphatic or blood supply.[4] The bacilli affect either the seminiferous tubules or Leydig cells. The levels of serum follicle-stimulating hormone (FSH), and luteinizing hormone (LH) are elevated, while levels of serum testosterone are depressed.[5] The hypofunction of the testis is due to the acute inflammatory exudate caused by leprous granuloma that results initially in sterility and later in impotence.[6] Testicular dysfunction leads to a deficiency in testosterone production, causing sexual dysfunction and an increased risk of osteoporosis.

Leprosy is an endemic disease in tropical areas of India. The endocrine manifestations secondary to leprosy are

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underestimated especially hypogonadism in male patients. There are few studies of testicular dysfunction in men with proven leprosy. Hence, we decided to conduct the study for evidence of hypogonadism through hormonal profile in males affected with leprosy.

Patients and Methods

Study design

This prospective observational study was conducted in the newly diagnosed male leprosy patients admitted to the Department of Dermatology, Venereology, and Leprosy from August to November 2022 at Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha, a rural tertiary care hospital located in Central India.

Study population

A total of 30 newly diagnosed male leprosy patients aged between 20 and 70 years undergoing treatment were enrolled in the study after obtaining written informed consent and approval from the institutional ethics committee for the study.

We excluded the patients with severe anemia, diabetes, on chemotherapy or radiotherapy, receiving treatment affecting fertility or hormones level, and the patient with immunocompromised conditions.

Laboratory investigation, including a 5 ml fasting blood sample (8 am to 10 am), was collected from each patient for evaluation of complete blood count, erythrocyte sedimentation rate, fasting and postprandial blood sugar level, serum FSH, LH, and testosterone level. Hormonal assay (FSH, LH, and testosterone) was done using a competitive chemiluminescent immune assay.

A structured prestructured questionnaire was used to collect data on clinic-epidemiological profile, thorough history taking, general examination, dermatological examination, and genital examination.

Diagnosis was confirmed by slit skin smear for acid-fast bacilli to estimate the bacillary index (BI) and was measured on a semiquantitative scale (0 to 6+) of Ridley[7] and histopathology from skin punch biopsies in our hospital.

Statistical analysis

The collected data were encoded and entered electronically in a computer Excel worksheet 2010 version. The statistical analysis was performed using SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA). Pearson correlation coefficient was calculated to examine the relationship between FSH, LH, and testosterone levels and also between BI, duration of disease, age, reaction, and hormonal level. The value of $P \leq 0.05$ was considered statistically significant.

Results

In the present study, the mean age of the leprosy patient was 41.93 ± 14.18 (the range of the age was 20–70 years). The mean duration of the disease was 2.67 ± 1.34 years (1 month to 6 years). In the present study, 30 male patients were clinically and histologically classified by Ridley–Jopling scale as follows: lepromatous leprosy (LL) (n = 9) (30%), borderline leprosy (n = 18) (60%), and tuberculoid leprosy (n = 3) (10%) [Table 1].

Testosterone and gonadotrophin levels in patients with leprosy

Out of a total of 30 patients, 18 (60%) patients had a lower level of testosterone (<300 ng/dL of normal for men), while 12 (40%) patients had a normal level of testosterone. 12 out of these 18 patients had a low level of testosterone without an increase in the level of FSH or LH. While in the remaining 6 (3 LL and 3 BL) patients, this low level of testosterone was seen with a higher level of FSH and/or LH. It signified that one-third of the leprosy patients (33.33%) had primary hypogonadism.

Out of nine LL patients, only three patients had a lower level of testosterone with a higher level of FSH and LH, three had normal testosterone with a high level of LH and FSH, while the remaining three had normal levels of FSH, LH, and testosterone levels. It signifies that one-third (33.33%)

Table 1: Characteristics of study participants (n=30)

Variables	Values
Mean age	41.93±14.18
Mean duration of the disease (years)	2.67±1.34
Patient clinically and histologically classified by Ridley–Jopling Scale, *n* (%)	
LL	9 (30)
Borderline leprosy	18 (6 BL, 9 BB, 3 BT) (60)
Tuberculoid leprosy	3 (10)
Marital status, *n* (%)	
Single	9 (30)
Married	21 (70)
Occupation, *n* (%)	
Unemployed	7 (23.3)
Service	5 (16.6)
Businesses	4 (13.3)
Others	14 (46.6)
BI	
<4	7
≥4	23
ENL	
Recurrent	9
Single	6
Absent	15
Reaction	
Type I	12
Type II	15
Absent	3
Mean testosterone level	
LL	301.17±168.9
Borderline leprosy	401.44±127.71

BL: Borderline lepromatous, BB: Mid borderline, BT: Borderline tuberculoid, LL: Lepromatous leprosy, ENL: Erythema nodosum leprosum, BI: Bacterial index

of LL patients had primary hypogonadism. In 18 borderline leprosy patients (6BL, 9BB, and 3BT), 15 had lower levels of testosterone, while 3 (BT) had normal levels of testosterone. Out of 15 patients with low testosterone levels, 3 (BL) patients had higher values of both FSH and LH, 3 (BL) patients had higher values of FSH only with normal LH value, while the remaining 9 (BB) patients had normal levels of both FSH and LH. It signifies that only one-sixth (16.67%) borderline leprosy patients had primary hypogonadism. Thus from single blood sample used for hormonal measurement, 33.33% of LL patient and 16.67% borderline LL patients had primary hypogonadism [Table 2].

Testosterone regulates the secretions of LH and FSH. Hence, we evaluated the relationship between a decrease in testosterone, LH and FSH. There was a negative correlation between LH and testosterone ($r = -0.25$, $P = 0.17$), FSH and testosterone ($r = -0.42$, $P = 0.02$), respectively [Figure 1a and b]. There was a positive correlation between FSH and LH levels ($r = 0.72$, $P < 0.00001$) [Figure 2], which was highly significant. This suggested patient to be affected by primary hypogonadism. Out of all 30 patients with bilateral testis, only three cases of LL and two cases of BL had testis, which were hard in consistency. The testes were slightly reduced in size than normal for that age. Only one patient of LL had orchitis. None of the patients had testicular atrophy and gynecomastia.

The relationship between hypogonadism and the disease state

FSH and LH levels were elevated 6 out of 9 LL patients, respectively (two-third, i.e., 66.67% of patients) and 6 FSH and 3 LH out of 18 in BL (33.33% and 16.67% of patients), respectively [Figure 3a and b]. Thus, patients with LL had more primary hypogonadism, as evidenced by elevated LH and FSH, than that of BL. The mean testosterone level was lower in LL patients (301.17 ± 168.9) compared to that of borderline patients (401.44 ± 127.71).

In the study population, BI increased from tuberculoid to the lepromatous pole of the disease spectrum. Patients with LL had significantly higher BI than those of BL, BB, and BT combined. There was positive correlation between BI and FSH ($r = 0.22$, $P = 0.22$), LH ($r = 0.15$, $P = 0.39$) [Figure 4a and b] and negative correlation between BI and testosterone level ($r = -0.07$, $P = 0.69$) [Figure 4c]. A positive correlation was found between age and duration of disease with FSH and

Table 2: Hormonal level of study participant and those with and without erythema nodosum leprosum

Variables	All subjects (n=30), n (%)	Subjects with ENL (n=15), n (%)	Subjects without ENL (n=15), n (%)
Serum testosterone			
Normal	12 (40)	6 (40)	6 (40)
Decreased	18 (60)	9 (60)	9 (60)
Serum FSH			
Normal	18 (60)	3 (20)	15 (100)
Elevated	12 (12)	12 (80)	0
Serum LH			
Normal	21 (30)	6 (40)	15 (100)
Elevated	9 (70)	9 (60)	0

ENL: Erythema nodosum leprosum, FSH: Follicle-stimulating hormone, LH: Luteinizing hormone

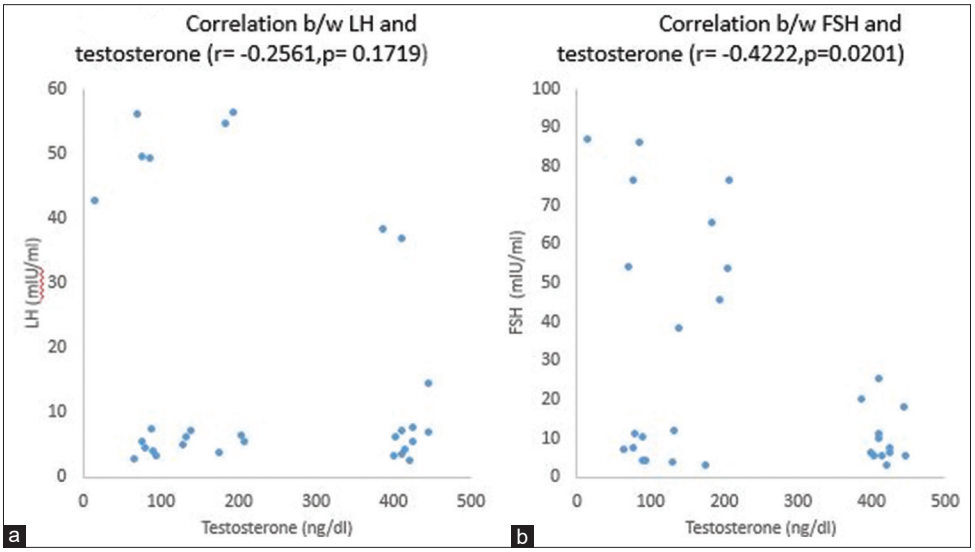

Figure 1: (a and b) Correlation between luteinizing hormone and follicle-stimulating hormone and testosterone levels. LH: Luteinizing hormone, FSH: Follicle-stimulating hormone

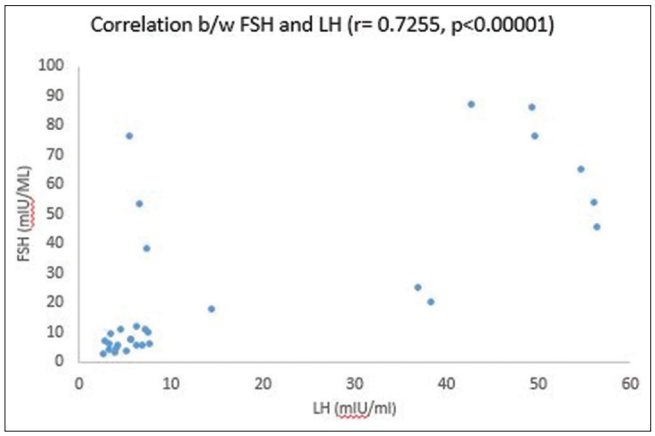

Figure 2: Correlation between follicle-stimulating hormone and luteinizing hormone levels. LH: Luteinizing hormone, FSH: Follicle-stimulating hormone

LH levels. However, when age and duration of disease were taken into consideration, there was a negative correlation with testosterone level [Figure 5a and b].

Of 30 patients, 21 presented with type 2 reaction, 6 with type 1 reaction, and 3 were not in reaction state. There was a significant positive correlation between reaction and FSH ($r = 0.41$, $P = 0.02$), LH ($r = 0.40$, $P = 0.02$), respectively [Figure 6a and b] and a negative correlation between reaction and testosterone ($r = -0.39$, $P = 0.03$) [Figure 6c] which was significant [Table 3].

The complete blood count showed hemolytic anemia, leukopenia, and lymphopenia, but those in reaction showed leukocytosis neutrophilia. Erythrocyte sedimentation rate was raised. Moreover, fasting and postprandial level were raised

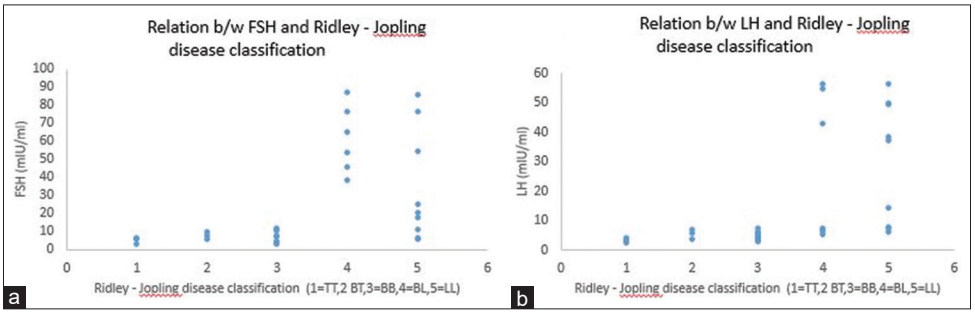

Figure 3: (a and b) Correlation between follicle-stimulating hormone and luteinizing hormone and Ridley–Jopling disease classification. LH: Luteinizing hormone, FSH: Follicle-stimulating hormone

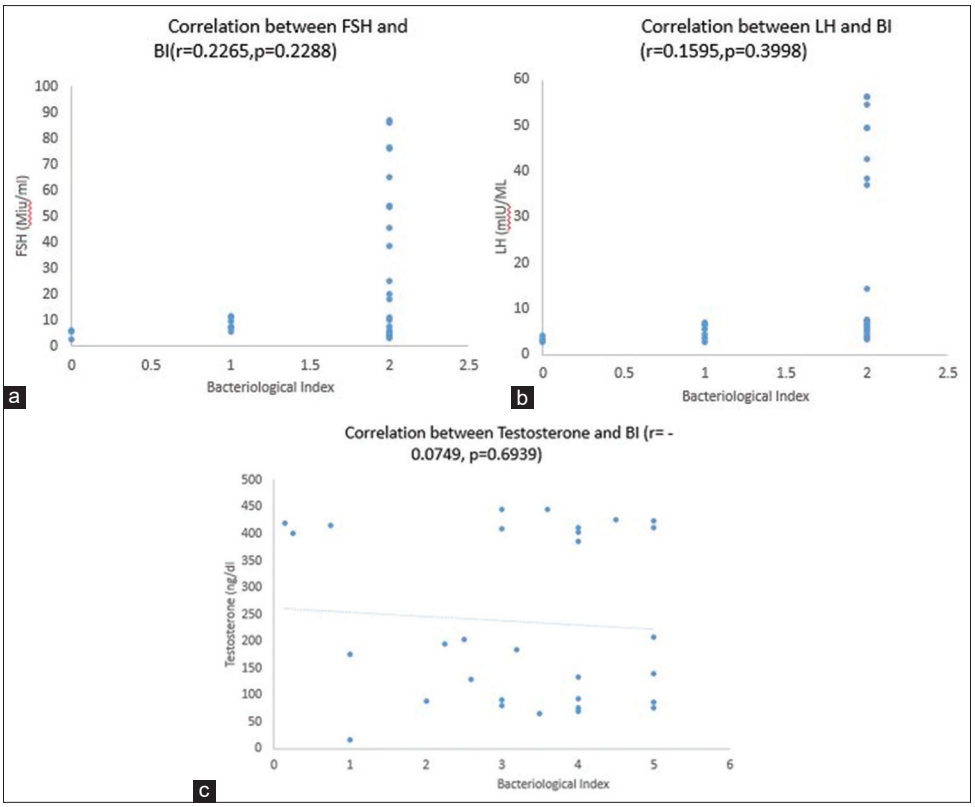

Figure 4: (a and b) Correlation between follicle-stimulating hormone and luteinizing hormone and bacterial index, (c) Correlation between testosterone and bacterial index. LH: Luteinizing hormone, FSH: Follicle-stimulating hormone

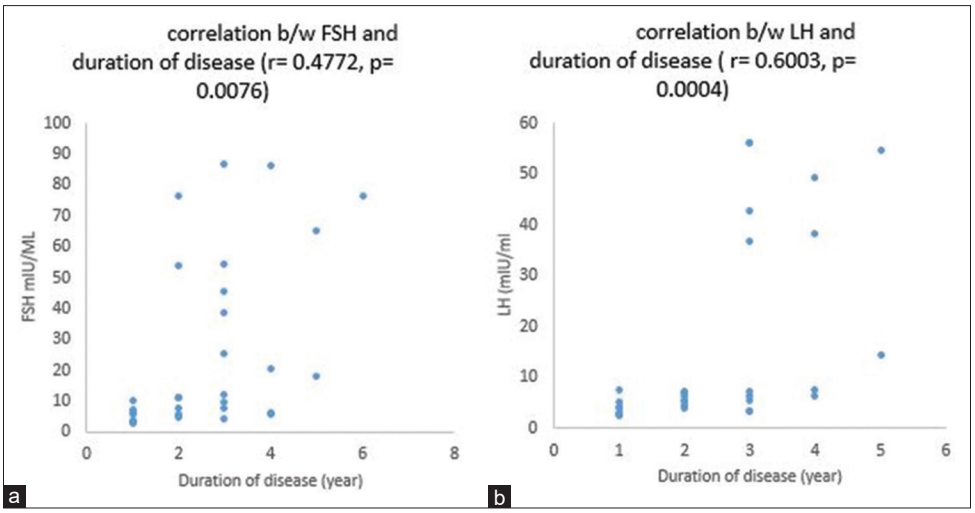

Figure 5: (a and b) Correlation between follicle-stimulating hormone and luteinizing hormone and duration of disease. LH: Luteinizing hormone, FSH: Follicle-stimulating hormone

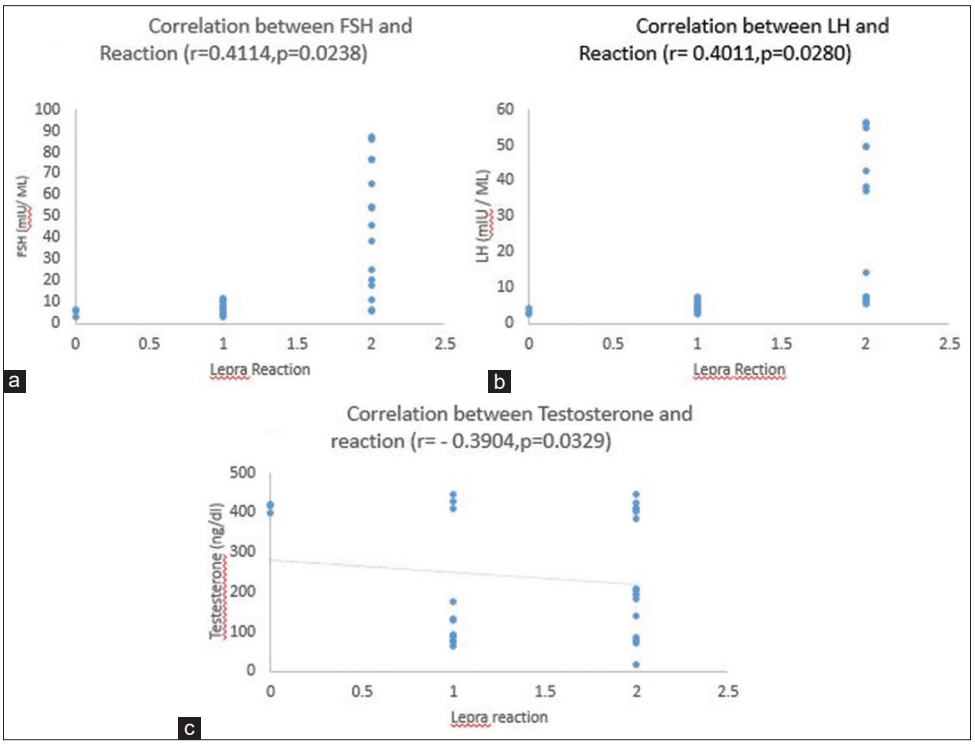

Figure 6: (a and b) Correlation between follicle-stimulating hormone and luteinizing hormone and reaction, (c) Correlation between testosterone and reaction. LH: Luteinizing hormone, FSH: Follicle-stimulating hormone

with those in reaction on oral corticosteroid, whereas it was normal in those without reaction.

Discussion

The testes are known to be a favored site for focal damage in patients with leprosy. This is probably because bacillary growth is favored at the lower temperature in the scrotum. The present study indicates that testicular dysfunction and primary hypogonadism are a consequence of leprosy in a significant number of lepromatous patients. More than one-third of the leprosy patients were affected with increased FSH and LH levels (as >18.1 and >9.3 mIU, respectively) and well-decreased levels of testosterone (<300 ng/dl). This is in correlation with the few studies that have shown changes in LH, FSH, and/or testosterone in lepromatous males.[2,5,6,8,9]

We observed that 3 out of 30 patients had elevated LH with normal testosterone, which may indicate early testicular atrophy. This can be because of the slight destruction of leydig cells. This is consistent with the finding of Hasan *et al*.[5] The damage to the seminiferous tubules leads to elevation of FSH

Table 3: Correlations of different variables

Variables compared	*R*	*P*
LH and testosterone	–0.2561	0.1719
FSH and testosterone	–0.4222	0.0201
FSH and LH level	0.7225	<0.00001
BI and FSH	0.2265	0.2288
BI and LH	0.1595	0.3998
BI and testosterone	–0.0749	0.6939
Duration and FSH	0.4772	0.0076
Duration and LH	0.6003	0.00045
Duration and testosterone	0.0415	0.8276
Reaction and FSH	0.4114	0.0238
Reaction and LH	0.4011	0.0280
Reaction and testosterone	–0.3904	0.0329
Age and FSH	0.1205	0.5257
Age and LH (LL)	0.4426	0.2329
Age and testosterone	–0.0641	0.7365

FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, BI: Bacterial index, LL: Lepromatous leprosy

levels. Testicular involvement in leprosy can occur in the absence of signs and symptoms.[10] Hence, serum testosterone, FSH, and LH should be measured repeatedly over the course of the disease to confirm testicular atrophy.[5]

In this study, there was a positive correlation between BI and FSH, LH levels and a negative correlation between BI and testosterone level. This finding was similar to the studies of Hasan *et al*.[5] and Gunawan *et al*.[9] This mainly signifies that testicular involvement occurs more toward lepromatous end of leprosy.

The study showed a positive correlation between age and duration of disease and FSH and LH as similar to Gunawan *et al*.[9] Serum testosterone level decreases with testicular involvement. Testosterone is one of the most important androgen hormones in males. Normally, as age advances, the testosterone level decreases in men. In leprosy, as age and duration of disease advances, there is decrease in testosterone and elevation of FSH and LH levels due to the involvement of Leydig cells and seminiferous tubules in testis. This can precede hypogonadism.

In the present study, none of the patients had gynecomastia and testicular atrophy. Only three patients of LL and two patients BL had hard testis with slightly reduced size. While, one patient of LL had orchitis. This was not similar to the study conducted by Abd-Elkawi *et al*.[6] and Gunawan *et al*.[9] where there was gynecomastia (25% and 6.25%, respectively) due to severe involvement of the testis. Many factors responsible for testicular function, which includes the degree of testicular involvement, frequency and intensity of orchitis and the immune complex disorder in leprosy. Other immune mechanisms also play a role in both the hypogonadism and infertility of lepromatous orchiopathy.[9]

There is a dearth in the literature regarding hypogonadism in male leprosy patients. We did not find any Indian study related to this topic, especially in Central India to date, as per our knowledge.

Conclusion

This study showed evidence of primary hypogonadism in leprosy patients. Furthermore, FSH, LH was elevated despite normal testosterone level, which indicates early testicular atrophy and early need for hormonal profile in a leprosy patient. Hence, it is recommended that leprosy (LL) patients should be routinely screened for hypogonadism using FSH, LH, and testosterone levels.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Desikan KV, Job CK. Visceral lesions caused by *M. leprae* – A histopathological study. Indian J Pathol Bacteriol 1970;13:100-8.
2. Singh RK, Bhasin R, Bisht YS, Kumar KV. Endocrine dysfunction in patients of leprosy. Indian J Endocrinol Metab 2015;19:369-72.
3. Leal AM, Magalhães PK, Souza CS, Foss NT. Adrenocortical hormones and interleukin patterns in leprosy. Parasite Immunol 2003;25:457-61.
4. Andrade LJ, Oliveira MF, Franca LS, Souza AL, Andrade CS, Jesus HB. Hypogonadism in leprosy males. Rev Cien Med Biol 2012;11:60-3.
5. Hasan M, Quyum F, Rahman MA, Panthi S. Testicular dysfunction in men affected by lepromatous leprosy. Lepr Rev 2017;88:258-64.
6. Abd-Elkawi FA, Bahgat SA, Kamel AM, Farag AS, Ashor OM. Testicular function in male patients with lepromatous leprosy. Egypt J Dermatol Venereol 2014;34:41-5.
7. Worobec SM. Treatment of leprosy/Hansen's disease in the early 21st century. Dermatol Ther 2009;22:518-37.
8. Singh N, Arora VK, Jain A, Bhattacharya SN, Bhatia A. Cytology of testicular changes in leprosy. Acta Cytol 2002;46:659-63.
9. Gunawan H, Achdiat PA, Rahardjo RM, Hindritiani R, Suwarsa O. Frequent testicular involvement in multibacillary leprosy. Int J Infect Dis 2020;90:60-4.
10. Leal AM, Foss NT. Endocrine dysfunction in leprosy. Eur J Clin Microbiol Infect Dis 2009;28:1-7.