Reproductive health in male systemic lupus erythematosus

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ABSTRACT

Objective: To assess reproductive health in male systemic lupus erythematosus (SLE) patients and compare them with controls. **Methods:** Twenty-five male SLE patients were evaluated for demographic data, urologic evaluation (including pubertal parameters, sexual/erectile function), testicular Doppler ultrasound, hormone profile, semen analysis, clinical features and treatment. The control group included 25 healthy men. **Results:** The current median age was similar in SLE patients compared with controls (26 *versus* 27 years, P = 0.756). The frequencies of sexual/erectile disfunction were significantly higher (20% *versus* 0%, P = 0.0001) and the number of spontaneous pregnancies were lower in SLE patients than in controls (20% *versus* 60%, P = 0.0086). A trend to low contraceptive use was observed in SLE patients compared with controls (48% *versus* 76%, P = 0.079). Moreover, the frequencies of gonadal dysfunction parameters, such as testicular atrophies measured by ultrasound (36% *versus* 8%, P = 0.037), elevated FSH and/or LH levels (36% *versus* 0%, P = 0.002), and sperm abnormalities (48% *versus* 0%, P = 0.0001), were statistically higher in SLE patients *versus* controls. SLE patients with sexual/erectile disfunction had no sexual activity in the last month *versus* 95% of SLE patients without dysfunction (P = 0.0001). On the other hand, no differences were evidenced in SLE patients with or without sexual/erectile disfunction according to demographic data, disease activity, cumulative damage and treatment. **Conclusion:** This is the first study to identify sexual/erectile and gonadal disfunction in male SLE patients. A multidisciplinary approach is essential in order to offer preventive measures for these patients.

Keywords: reproductive health, sexual function, sperm, hormone, systemic lupus erythematosus, male.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease which presents a minor prevalence in the male gender, typically affected during the reproductive period.[1] Novel therapeutic options have also improved the survival of men with SLE and reinforced the importance of quality of life, including aspects related to the testicular function evaluation and reproductive health, like puberty marks, sexual function and infertility.[2-5]

Recently, our group evaluated various parameters of gonadal function in 35 men with SLE and identified seminal alterations (median reductions of: concentration, motility, and normal forms of the spermatozoids), testicular atrophies and elevations of the follicle-stimulating hormone (FSH)

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associated to therapy with endovenous cyclophosphamide.[6] Later, we studied the function of Sertoli testicular cells by assessing the inhibin B serum levels in 34 patients with SLE and evidenced lower levels of this hormone in patients treated with endovenous cyclophosphamide in comparison with those who did not use this drug.[7] Nevertheless, a global evaluation of all reproductive health parameters and its comparison with the control group healthy men has not been done yet.

On the other hand, there are rare reports in the medical literature about reproductive health alteration in male adolescents, youngsters and adults with SLE, which include the description of delay of puberty marks and spermarche[2,3] as well as sexual and/or erectile disfunctions.[2,8-10] However, in their evaluations none of these studies adequately used the term infertility as it is preconized by the World Health Organization (WHO). In fact, the WHO reinforces the necessity of couple's evaluation and defines infertility as the absence of conception after a consecutive period of 12 months of frequent sexual activity, without the utilization of contraceptive methods.[11]

Therefore, the objective of the present study was to evaluate the possible association between reproductive health parameters (including the evaluation of the gonadal function) in men with SLE and compare them with healthy controls. Besides that, we tried to establish possible associations between demographic data, reproductive health parameters, disease activity, cumulative damage and treatment used in patients presenting sexual and/or erectile dysfunctions.

PATIENTS AND METHODS

1. Patients with SLE and healthy controls

Seventy five male patients with ages between 15 and 45 years, followed-up in the Pediatric Rheumatology Unit of the Instituto da Criança (ICr) and in the Lupus Clinic of the Rheumatology division of the Hospital das Clínicas (HC) – Faculdade de Medicina at Universidade de São Paulo (FMUSP), were selected for this study between January of 2003 and January of 2006. All patients fulfilled the classification criteria for the diagnosis of SLE proposed by the American College of Rheumatology.[12] The exclusion criteria were hydrocele, hypospadia, cryptorchism, testicular infection by mumps, testicular cancer, orchitis, testicular vasculitis, ureteral disfunction, previous history of scrotal or inguinal surgeries, *diabetes mellitus*, previous history or current use of alcohol or smoking, and refusal to collect semen sample or incomplete evaluation. At the end of the study, 50 patients were excluded: refusal (n = 31), incomplete evaluation (n = 17), and previous vasectomy (n = 2).

For comparison with the 25 patients with SLE included in the study, a control group was formed of 8 healthy adolescents regularly followed in the Adolescent Unit of the ICr-HC-FMUSP and 17 fertile adults planning vasectomy in the Division of Urology of HC-FMUSP. The Research and Ethics Commission of HC-FMUSP approved the study, and an informed consent form was obtained from all the participants and, when necessary, of their representatives.

2. Evaluation of the reproductive health

2.1 Clinical history and urologic examination

These evaluations included demographic data (age at the beginning of the disease, duration of SLE, and current age), age at the first perceived ejaculation (spermarche by masturbation, sexual activity, or involuntary ejaculation),[6] age at the beginning of sexual activity, performance and number of sexual activity in the last month, number of partners with gestations, presence of sexual or ejaculatory disfunctions by clinical history (reduced libido, erectile disfunction, premature ejaculation, absence of orgasm [anorgasmy] and/or dissatisfaction of the sexual life), use of male contraceptive in sexual relations (preservative or male condom). Infertility, according to the criteria of WHO, was defined as the absence of conception after a consecutive period of 12 months of frequent sexual activity, without the utilization of contraceptive methods.[11]

A systematic clinical examination of the genitalia was performed in patients and controls by only one andrologist from the Human Reproduction Center of HC-FMUSP and included testicles evaluation, epididymis, vas deferens, scrotum and penis.[6] The sexual characteristics were determined in agreement with criteria proposed by Tanner for pubertal alterations (pubic hair distribution and characteristics of the genitalia).[13] The testicular volumes were measured using a Prader orchidometer, which consists of 12 ellipsoid models graded from 1 to 25 mL (1 to 6, 8, 10, 12, 15, 20, and 25 mL).[14] In postpubertal adolescents and adult males, testicular atrophy by Prader was defined as when the testicular volume was inferior to 12 mL.[15] Varicocele was classified according to grades: grade I (minor) – palpable only with Valsalva's maneuver; grade II (medium) – palpable with the patient in orthostatic position; and grade III (major) – visible through the scrotum skin and palpable with the patient in dorsal decubitus.[6]

2.2 Evaluation of the gonadal function

2.2.1 Testicular ultrasonography with Doppler: Testicular ultrasonography was performed in all patients and controls by the same ultrasonographer from the Department of Radiology

of HC-FMUSP, a testicular examination specialist, using a 14-MHz scanner (Logic 9-GE – Milwaukee, Wisconsin, USA), in a blind manner to the reproductive health analysis and other parameters of the gonadal function. Testicles were measured in the axial and longitudinal planes, and at least two measurements of width, length and thickness were obtained. The higher measure of each dimension was recorded and used to calculate the testicular volume according to the formula: width × length × thickness × 0.52. In postpubertal adolescents and male adults, testicular atrophy by testicle ultrasonography was defined when the testicular volume was inferior to 7 mL.[19]

2.2.2 Hormonal profile and primary hypogonadism: The hormonal determinations were performed at the beginning of the study in the Medical Investigation Laboratory (LIM 36) of the Department of Pediatrics of FMUSP. Abnormal results were repeated for confirmation. FSH, luteinizant hormone (LH) and total testosterone were evatulated by immunofluorescence using the DELPHIA^{R} time-resolved fluoroimmunoassay kits (WALLAC Ou, Turku, Finland). The variation coefficients intra- and interanalysis were 3.5% and 2.1%, respectively. Normal values were: FSH (1-10.5 IU/L), LH (1-8.4 IU/L) and total testosterone (271-965 ng/dL). Primary hypogonadism was defined as elevated serum levels of hypophyseal gonadotrophins (FSH and/or LH) and reduced serum levels of total testosterone.[17]

2.2.3 Spermatozoids alterations: Semen analysis was performed in agreement with the WHO guidelines[11,18] by two experienced biomedical scientists from the Human Reproduction Center of HC-FMUSP, in a blind manner to the other parameters of reproductive health and gonadal function. All patients and controls collected two semen samples by masturbation in a collection room that were processed within one hour of liquefaction, after 48 to 72 hours of sexual abstinence, in the period of up to one month after the admission to the study. The samples were analyzed by manual count as well as by the computer-assisted semen analysis system with an enhancement of 400X, using a HTM-2030 (Hamilton Thorne Research, Beverly, Massachusetts, USA). Each apparatus was scanned to estimate the number of spermatozoids by field equivalent to 1 mL, to obtain a spermatozoid concentration approximated in millions of spermatozoids by milliliter of semen. The spermatozoid motility was determined through the analysis of at least five microscopic fields in a systematic manner to classify 200 spermatozoids. The morphology of the spermatozoids included the evaluation of the spermatozoid's head, neck, intermediary piece and tail by two biomedical scientists who did not know the other parameters of reproductive health and gonadal function in patients and controls.[11] Oligozoospermia was defined as when the spermatic concentration was < 20 millions/mL, astenozoospermia as when the spermatozoid motility was < 50%, teratozoospermia as when the normal spermatozoid morphology was < 15% according to WHO and oligoastenoteratozoospermia was defined by alterations in the three variables.[11] Spermatozoid morphology was also evaluated in agreement with Kruger's strict criteria, in which normal morphology < 14% is associated to subfertility.[19]

2.2.4 Antispermatozoid antibodies: The evaluation of antispermatozoid antibodies were performed at the beginning of the study in the Human Reproduction Center of HC-FMUSP. These were determined by direct Immunobead test which uses reagents containing rabbit immunoglobulins directed against human antispermatozoid antibodies (IgA, IgG, and IgM) (Irvine Scientific, Santa Ana, California, USA). The direct tests with labelled antibodies detect antibodies that bind to the cellular surface of spermatozoid (head of the spermatozoid, intermediary part and/or tail). At least 50% of the moving spermatozoids should be covered with marked antibodies before the test is considered clinically significant.[11] Quality control was defined as recommended by the manufacturer.

3. Evaluations of SLE activity, disease's cumulative damage and treatment

The disease activity and the cumulative damage of SLE were evaluated in all patients at the beginning of the study, using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)[20] and Systemic Lupus International Collaborating Clinics/ACR-Damage Index (SLICC/ACR-DI) scores, respectively.[21] Data referring to the treatment with prednisone, ciclophosphamide, azatioprine and methotrexate were determined.

4. Statistical analysis

The results were presented in median (variation) for continuous variables and number (%) for categorical variables. The results were compared by t- and Mann-Whitney tests for continuous variables to determine the difference between patients with SLE *versus* controls and between patients with SLE according to two groups: with and without sexual and/or erectile disfunction. For categorical variables, differences were calculated by Fisher's exact test. Values of $P < 0.05$ were considered statistically significant.

RESULTS

Aspects of the reproductive health and gonadal function in patients with SLE *versus* healthy controls

The current age was similar between patients with SLE and the control group (26 *versus* 27 years, P = 0.756). All patients and controls presented the last pubertal Tanner stage (P5G5),[13] with adult pubic hair reaching the internal surface of the thighs and adult genitals in shape and size (100% *versus* 100%, P = 1.0). There was not any statistical difference in relation to the age of spermarche in both groups (13 *versus* 12 years, P = 0.168). The first perceived ejaculation occurred predominantly by masturbation in both groups (68% *versus* 60%, P = 0.768). The demographic data, reproductive health aspects of men with SLE *versus* controls are in Table 1.

Regarding the aspects of the reproductive health, sexual/erectile disfunction (presence of reduced libido, erectile disfunction, premature ejaculation and/or anorgasmy) and dissatisfaction with sexual life were reported in 20% of the patients with SLE and in none of the controls (P = 0.0001 and P = 0.0001, respectively). In addition, the percentage of partners with gestations was statistically lower in SLE patients compared with controls (20% *versus* 60%, P = 0.0086). There was a statistical tendency to lower frequency of male preservatives use between SLE and controls (48% *versus* 76%, P = 0.079). On the other hand, there was not a statistical difference regarding the age of spermarche, age of first sexual activity, performance and number of sexual activities in the last month, as well as the presence of decreasing libido, erectile disfunction, premature ejaculation and anorgasmy in patients with SLE *versus* healthy controls (P > 0.05) (Table 1).

A relevant aspect of the present study was that the diagnosis of infertility according to WHO criteria was established in only one couple whose man had SLE and in none healthy control (P = 1.0). This SLE patient's wife was evaluated in the Human Reproduction Center of HC-FMUSP. She had ovulatory menstrual cycles without previous history of abortion, and all complementary examinations preconized for her evaluation were normal: pelvic ultrasonography and hormones (thyroidal, FSH, LH, estradiol, and prolactin). The SLE patient had an inactive disease and did not use cyclophosphamide. He presented erectile dysfunction, although all parameters of the gonadal function were normal (exception to teratozoospermia). He was directed to use sildenafil citrate 25 mg, 30 minutes before sexual activity, with posterior normalization of erection. He is being followed-up in the Human Reproduction Center of HC-FMUSP and without occurrence of spontaneous pregnancy yet.

Concerning gonadal function parameters, 60% of SLE patients *versus* none of controls presented spermatozoids alterations [azoospermia (absence of spermatozoids) or teratozoospermia (abnormal morphology of spermatozoids) associated with oligozoospermia (low spermatozoid concentration) and/or asthenozoospermia (low spermatozoid motility)] (P = 0.0001). Testicular atrophy at ultrasonography and elevations in the hypophyseal gonadotrophins (FSH and/or LH) were significantly more evidenced in the SLE patients when compared with controls (36% *versus* 8%, P = 0.037 and 36% *versus* 0%, P = 0.002; respectively). Nevertheless, in both groups there was not a statistically significant difference regarding the frequencies of other gonadal function parameters: testicular atrophy by Prader, primary hypogonadism, reduction of total testosterone and presence of antispermatozoid antibodies (P > 0.05). Also there was no statistical difference regarding the presence of varicocele grade I or II in SLE patients *versus* controls (P > 0.05) (Table 1).

Aspects of reproductive health and gonadal function in SLE patients with and without sexual and/or erectile disfunction

Demographic data, aspects of reproductive health, disease's activity, cumulative damage of the disease and treatment of men with SLE with and without sexual/erectile dysfunction are in Table 2.

Onset age of SLE (15 *versus* 20 years, P = 1.0), duration of the disease (13 *versus* 8 years, P = 0.316) and current age (29 *versus* 26 years, P = 0.795) were similar between patients with SLE with and without sexual/erectile dysfunction. Sexual activity in the last month was not reported by none of the SLE patients with sexual and/or erectile disfunction *versus* 95% of those with normal function (P = 0.0001). SLE patients who presented sexual and/or erectile disfunction had a significant frequency of erectile disfunction (40% *versus* 0%, P = 0.033), premature ejaculation (40% *versus* 0%, P = 0.033), anorgasmy (40% *versus* 0%, P = 0.033) and sexual dissatisfaction (100% *versus* 0%, P = 0.0001) compared with patients with normal function (Table 2).

Nevertheless, there was not any statistical difference in relation to medians or frequencies of: spermarche age, Tanner's pubertal stage (P5G5),[13] onset age of sexual activity, partners with gestations and use of male preservative between patients with SLE who reported sexual and/or erectile disfunction *versus* normal ones. In addition, in both groups there were not statistically significant differences regarding frequencies of gonadal function parameters: testicular atrophy

Table 1
Demographic data, aspects of reproductive health of men with systemic lupus erythematosus (SLE) *versus* controls

Variables of reproductive health	SLE (n = 25)	Controls (n = 25)	P
Demographic data			
Current age, years	26 (15-45)	27 (15-54)	0.756
Pubertal signs and sexual function			
Age of spermarche, years	13 (12-13)	12 (11-15)	0.168
Spermarche by masturbation	17 (68)	15 (60)	0.768
Tanner pubertal stage P5G5	25 (100)	25 (100)	1.0
Onset Age of sexual activity, years	15 (12-21)	16 (12-24)	0.629
Sexual activity in the last month	20 (80)	24 (96)	0.189
Number of sexual activities in the last month	4 (0-30)	8 (0-16)	0.139
Partners with spontaneous gestations	5 (20)	15 (60)	0.0086
Sexual and/or erectile disfunction	5 (20)	0 (0)	0.0001
Reduced libido	1 (4)	0 (0)	1.0
Erectile disfunction	2 (8)	0 (0)	0.49
Premature ejaculation	2 (8)	0 (0)	0.49
Anorgasmy	2 (8)	0 (0)	0.49
Dissatisfaction with sexual life	5 (20)	0 (0)	0.0001
Use of male preservative	12 (48)	19 (76)	0.079
Infertility	1 (4)	0 (0)	1.0
Gonadal function			
Testicular atrophy by Prader (R and/or L)	6 (24)	1 (4)	0.098
Testicular atrophy by US (R and/or L)	9 (36)	2 (8)	0.037
Varicocele grade I or II	6 (24)	2 (8)	0.246
Primary hypogonadism	2 (8)	0 (0)	0.49
Total testosterone < 271 ng/dL	4 (16)	1 (4)	0.349
FSH > 10.5 UI/L and/or LH > 8.4 UI/L	9 (36)	0 (0)	0.002
Spermatozoids alterations*	12 (48)	0 (0)	0.0001
Antispermatozoid antibodies > 50%	1 (4)	0 (0)	1.0

Values are expressed in n (%) or median (variation), P – pubic hair, G – genitalia, R – right, L – left, US – testicular ultrasonography, FSH – follicle-stimulating hormone, LH – luteinizant hormone. *Patients with azoospermia (absence of spermatozoids) or teratozoospermia (abnormal morphology of spermatozoids) associated with oligozoospermia (low spermatozoid concentration) and/or asthenozoospermia (low spermatozoid motility).

by Prader and ultrasonography, primary hypogonadism, total testosterone reduction, spermatozoids alterations and presence of antispermatozoid antibodies (P > 0.05). Also there was no statistical difference in relation to the presence of varicocele grade I or II in the two groups (P > 0.05) (Table 2).

The SLEDAI [0 (0-12) *versus* 0 (0-6), P = 0.295] and SLICC/ACR-DI [0 (0-1) *versus* 0 (0-3), P = 0.36] medians were similar in SLE patients with sexual and/or erectile dysfunction in comparison with those with normal function. The frequencies of prednisone and immunossupressors use (ciclophosphamide, azatioprine, and methotrexate) were also similar in both groups (P > 0.05) (Table 2).

DISCUSSION

This is the first study in medical literature that simultaneously evaluated aspects of reproductive health and testicular function in SLE and identified the presence of sexual/erectile dysfunction in men with lupus when compared with controls at same pubertal stage. Despite the higher prevalence of seminal parameters alterations and the lower frequency of spontaneous gestations in partners of SLE patients, infertility was rarely evidenced in this population.

In this study, male sexual function includes characteristics of clinical history data, as it is suggested by WHO for evaluation

Table 2
Demographic data, aspects of reproductive health, activity, cumulative damage of the disease and treatment of men with systemic lupus erythematosus (SLE) with and without sexual/erectile disfunction

Variables of reproductive health	SLE with sexual/ erectile disfunction (n = 5)	SLE without sexual/ erectile disfunction (n = 20)	P
Demographic data			
Onset age of SLE	15 (13-36)	20 (2-40)	1.0
Duration of SLE	13 (4-19)	8 (2-20)	0.316
Current age, years	29 (23-38)	26 (15-45)	0.795
Pubertal signs and sexual function			
Age of spermarche	13.5 (13-15)	13 (12-15)	0.187
Tanner pubertal stage P5G5	5 (100)	20 (100)	1.0
Onset age of sexual activity, years	15.5 (15-19)	15 (12-21)	0.434
Sexual activity in the last month	0 (0)	20 (95)	0.0001
Reduced libido	1 (20)	0 (0)	0.2
Erectile disfunction	2 (40)	0 (0)	0.033
Premature ejaculation	2 (40)	0 (0)	0.033
Anorgasmy	2 (40)	0 (0)	0.033
Dissatisfaction with sexual life	5 (100)	0 (0)	0.0001
Partners with spontaneous gestations	1 (20)	4 (20)	1.0
Use of male preservative	3 (60)	9 (45)	0.644
Infertility	1 (20)	0 (0)	0.2
Gonadal function			
Testicular atrophy by Prader (R and/or L)	0 (0)	6 (30)	0.287
Testicular atrophy by US (R and/or L)	1 (20)	8 (21)	0.620
Varicocele grade I or II	0 (0)	6 (29)	0.540
Primary hypogonadism	1 (20)	1 (5)	0.366
Total testosterone < 271 ng/dL	1 (20)	3 (15)	1.0
FSH > 10.5 UI/L and/or LH > 8.4 UI/L	3 (60)	6 (30)	0.312
Spermatozoids alterations*	3 (60)	9 (45)	0.644
Antispermatozoid antibodies > 50%	1 (20)	0 (0)	0.2
Activity and cumulative damage of SLE			
SLEDAI	0 (0-12)	0 (0-16)	0.295
SLICC/ACR-DI	0 (0-1)	0 (0-3)	0.360
Therapeutics of SLE			
Prednisone	4 (80)	20 (100)	0.2
Cyclophosphamide	2 (40)	9 (45)	1.0
Azatioprine	4 (80)	11 (55)	0.614
Methotrexate	1 (20)	6 (30)	1.0

Values are expressed in n (%) or median (variation), P – pubic hair, G – genitalia, R – right, L – left, US – testicular ultrasonography, FSH – follicle-stimulating hormone, LH – luteinizant hormone. *Patients with azoospermia (absence of spermatozoids) or teratozoospermia (abnormal morphology of spermatozoids) associated with oligozoospermia (low spermatozoid concentration) and/or astenozoospermia (low spermatozoid motility). SLEDAI – Systemic Lupus Erythematosus Disease Activity Index, SLICC/ACR-DI – Systemic Lupus International Collaborating Clinics/ACR Damage Index.

of male infertility,[11] which includes aspects of erectile (erection maintenance), orgastic (reaching orgasm), and ejaculatory function besides libido (sexual desire or will) and satisfaction with sexual life as a whole.[2] Difficulties in sexual intercourse or ejaculation can cause infertility in 2% of the couples,[11] but this was evidenced in only one patient in this study who obtained resolution with sildenafil. The rare studies that evaluated the sexual function of SLE men did not have a control group and usually included both sexes, but none of those performed a concomitant evaluation of gonadal function. Stein *et al.*[8] evidenced that 4% of women and men with SLE presented sexual dysfunctions by clinical history data. Folomeev & Alekberova[9] identified a high frequency of sexual/erectile disfunction (alteration in the libido, erection and/or ejaculation) in 17/48 (35%) men with SLE. Erectile disfunction occurred in 7/17, however only two had dysfunction after the onset of SLE, which was not related with disease activity and immunosuppressive medications, as observed in the present study.

The sexual/erectile disfunction in men with SLE is multifactorial and can occur by the disease activity itself (with reduction of libido and frequency of sexual activity) or by medications, such as corticosteroids and immunosuppressors, and can determine a primary hypogonadism with male sexual hormone reduction.[2] In spite of the absence of statistically significance between sexual and/or erectile disfunctions *versus* activity, cumulative damage and treatment of the disease, other possible causes of these dysfunctions that were not researched in the present study are: low self-esteem and stress caused by the chronic disease itself, associated depression, as well as ununderstanding, and lack of partner support in sexual act.

An interesting aspect observed in the present study was that SLE patients initiated their sexual activity early (median of 15 years), just like healthy men. This was also verified in our study with female adolescents with lupus, in which the onset age of sexual life was similar to controls (mean of 15.3 years).[22] The same was observed in adolescents with other chronic diseases, as we evidenced in patients with epilepsy (median of 15 years).[23]

We also observed that male preservative use in routine sexual relations happened only in half of SLE men in this study, similarly to the 59% use of contraceptives by SLE American adolescents.[10] This risk behavior can lead, undoubtedly, to a greater risk of sexually transmitted diseases, including acquired immunodeficiency syndrome (AIDS)[2] and human papillomavirus (HPV).[22] These data are also relevant for female adolescents with SLE, since the practice of unsafe sexual activity has increased the numbers of unwanted and unplanned pregnancies among patients, as verified in a recent national multicentric study in 12 Pediatric Rheumatology Services.[24]

In the present study, a delay in the age of first ejaculation in SLE patients was not observed and it goes against what was identified in female SLE patients whose menarche occurred approximately one year after expected, comparing with Brazilian healthy adolescents.[22,25,26] Nevertheless, the accuracy of spermarche and first sexual activity ages in urologic history is questionable. It differs from menarche age, which is a definite mark in women reproductive life.

It is important to emphasize that the evaluation of testicular volume is an essential step in the evaluation of gonadal function once the seminiferous tubules represent 95% of testicular volume and are correlated with spermatogenesis.[4] The important reduction of testicular volume observed at ultrasonography, correlated to semen normalities severity, suggests a severe lesion of the seminiferous tubules in lupus. Also, levels of pituitary gonadotropins were higher in SLE patients. In fact, FSH is the main marker of seminiferous epithelium,[27] and elevated levels suggest testicular lesion, as it was previously evidenced by our group. It reinforces the need of seminal cryopreservation, particularly before cyclophosphamide.[6]

Varicocele is one of the main causes of male infertility; however, grades I and II may not present spermatozoid abnormalities and usually do not determine alterations in hypothalam-hypophysis-gonads axis and sexual disfunction.[4] Another relevant aspect is that, even with testicular dysfunction observed in our study, most patients (80%) still have satisfactory sexual function.

This research included a wide evaluation of reproductive health, particularly pubertal signs, sexual and testicular functions, which may be useful to the rheumatologist practice. Nevertheless, future studies utilizing specific sexual function instruments, validated in Brazilian male population with lupus, will be necessary,[28] besides the global evaluation the sexual function among their partners.

The findings suggest that reproductive health and gonadal function in men with SLE are affected during their reproductive years. A multidisciplinary approach, including urological and psychological evaluations, is essential for a better quality of life of the patients and their partners.

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