

Hypogonadism and erectile dysfunction in patients with chronic kidney disease undergoing hemodialysis

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Abstract

Objective: To know the profile of Hypogonadism and Erectile Dysfunction (ED) in patients with chronic kidney disease (CKD) on hemodialysis studied. **Method:** The case-control study was the Case group, consisting of patients with CKD on hemodialysis (INEFRO) and the Control group by patients under outpatient follow-up. The Androgenic Deficiency in Aging Males (ADAM) and International Index of Erectile Function (IIEF) questionnaires were applied, and the following clinical examinations were performed: orchidometry, analysis of hair distribution, gynecomastia and BMI. **Results:** ADAM's mean score was 4.2 points (case) and 1.9 points (control). In the Case group 60% have observed decreased libido and 70% perceived that the erections are less vigorous. In the Control group, prevalence decreased to 30% in both questions. In the analysis of IIEF-5, the mean score was 16.63 (case) and 19.93 (control). 60% of patients in the Case group and 50% of the Control group have some degree of ED. Gynecomastia was evaluated in 20% (case) and 7% (control). The orchidometry of the Case group revealed prevalence in 53.33% of testicular volume 3 patients of the orchidometer. In the control group, the most prevalent measure was 4, found in half of the patients (50%). **Conclusions:** Through the questionnaires applied in both groups with similar mean ages, it can be inferred that patients in the Case group experienced earlier, throughout the dialysis process, a direct impact on sexual quality, with decreased libido and difficulty in the reaction when compared to the Control group.

Keywords: Hypogonadism; quality of life; Chronic kidney disease; Erectile dysfunction

1. Introduction

Chronic Kidney Disease (CKD) has a significant prevalence in public health worldwide. In the UK it is estimated the ratio of 100 chronic kidney disease patients / 1,000,000 inhabitants and an annual growth of 5% to 8% is expected [1;2]. In the USA, this ratio rises to 336 chronic kidney patients / 1,000,000 inhabitants [3;2]. CKD is characterized by the functional and structural loss of nephrons, which are responsible for filtering the blood, in order to debug metabolites, such as urea, which become expendable to the human organism. In addition to excretion, the kidneys play a key role in the acid-basic balance and endocrine functions such as: the production of erythropoietin – hormone responsible to produce erythrocytes, renin – hormone linked to the renin-angiotensin-aldosterone system that influences the control of blood pressure, among others.

Comorbidities such as hypertension (SAH) and diabetes mellitus (DM) are the main causes of CKD, representing more than 70% of cases that progress to end-stage kidney disease in the United States of America [4]. The increase in life expectancy of Brazilians also contributes to this evolution.

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As expected, course of chronic kidney disease, patients who reach stages 4, characterized by clinical or severe renal disease phase, and 5, known as phase of chronic kidney disease with glomerular filtration rate lower than 15 ml/min, experience the lack of control of metabolic and endocrine functions, generating a uremic environment. For these patients, renal replacement therapy, either through dialysis or kidney transplantation, becomes necessary for maintenance of homeostasis [5].

According to data from the 2017 Dialysis Census published by the Brazilian Society of Nephrology [6], the number of dialysis patients in Brazil almost tripled in the period from 2000 to 2017, from 42,695 to 126,583 Brazilians, with a prevalence of 58% male and aged 45 to 64 years (42.6%).

Uremia in these patients may alter lipid, protein and glucose metabolism, cause anemia, malnutrition and important hormonal disorders, among them are altered the hormones of the hypothalamus-pituitary axis, mainly gonadotropins (luteinizing hormone [LH] and follicle stimulating hormone [FSH]) and prolactin (hyperprolactinemia) [7].

Communication between the central nervous system and the endocrine system is made through the axis between the hypothalamus and the anterior pituitary gland. The hypothalamus secretes factors that stimulate or inhibit adenohypophysis, and that regulate the rate of secretion of pituitary hormones such as growth hormone (GH), adrenocorticotropic hormone (ACTH), thyroid hormone (TSH), prolactin and gonadotrophic hormones (LH and FSH).

LH and FSH are glycoproteins controlled by gonadotropins-releasing hypothalamic hormone (GnRH) and by the feedback mechanism of steroids such as testosterone and peptides such as inhibin, which is produced by Sertoli cells, located in the seminiferous tubules. Testosterone is responsible for the negative feedback of LH in the pituitary and hypothalamic levels, while inhibin is responsible for the feedback of FSH in the pituitary gland.

Another hormone that performs negative feedback on the release of gonadotropins is prolactin. In patients with renal dysfunction, the metabolism of this hormone is impaired, considering that about 25% of its metabolization is renal. Hyperprolactinemia constitutes the most common change in the hypothalamic-pituitary axis and is related to impaired sexual potency and reduced libido [5]. This increase in prolactin can cause hypogonadism by inhibiting the release of the hormone stimulating gonadotropins (GnRH) by the hypothalamus [8]. DOURADO 2016, points out that hyperprolactinemia in CKD can range from 30% to 65% of cases [9;10].

Thus, there is less stimulation of the adenohypophysis to produce gonadotropins. At the testicular level, LH acts on Leydig cells to produce and release the androgenic hormone testosterone, while FSH acts on spermatogenesis and stimulates the development of seminiferous tubules. As a consequence of this change in the axis, it is known that total serum testosterone presents in lower concentrations in chronic renal patients [11]. This laboratory profile when associated with clinical signs and symptoms is called hypogonadotropic hypogonadism.

According to the Guideline of the European Association of Urology (2012) [12], hypogonadism consists of a syndrome caused by androgen deficiency, which can present the following clinic manifestations: decreased libido, erectile dysfunction (ED), obesity, gynecomastia, loss of muscle mass, fatigue, bone demineralization, infertility, abnormal distribution of hair, testicular decrease, depression, sleep disorders, among others. This clinical condition is classified as primary or secondary and may present congenital or acquired etiologies. In primary forms, hypogonadism has testicular origins. Causes such as cryptorchidism, testicular malignancy, medications, orchitis and systemic diseases fit this follow-up. In these cases, serum testosterone is below 300 ng/dL [13], but the serum concentrations of LH remain within the normal range, so it is called hypergonadotropic. In secondary forms, hypogonadism is hypogonadotropic, as it is characterized by a dysfunction of the hypothalamic-pituitary axis and, consequently, decreased serum concentration of LH < 9.4 IU/L [14;15], in addition to low testosterone levels, already mentioned. Hyperprolactinemia, kidney failure, hemochromatosis, hypothyroidism, Kallmann syndrome, trauma and obesity are the possible causes of this type of hypogonadism [12].

It is known that one of the probable consequences of both hypogonadism and CKD is the erectile dysfunction [16;17] which is characterized by persistent difficulty in obtaining and/or maintaining a sufficient erection for satisfactory sexual performance [18]. It occurs because plasmatic levels of testosterone are low, and in CKD patients, in general, have associated comorbidities such as DM, SAH, dyslipidemias and anemia, which also contribute to sexual impotence. It is estimated that ED is present in 80% of CKD cases [19].

ED can occur by three basic mechanisms: the difficulty of initiating the erection (neurogenic, endocrine, and psychogenic), difficulty in penile filling (arteriogenic) and difficulty in maintaining adequate intracavernous blood volume (occlusive vascular alteration) [11]. In relation to neurogenic disorder, common neuropathy in chronic kidney

patients prevents the parasympathetic stimulation to the sacral level, not allowing the relaxation of the penile smooth muscle and, consequently, there is no blood accumulation in the cavernous bodies. The endocrine alterations are related to the dysfunction of the hypothalamus-pituitary axis that led to low production of androgens, which are responsible for libido and ejaculatory volume. Psychogenic factors [20;11] include stress, depression, low self-esteem that can follow the routine of a dialysis patient, who 2 to 3 times a week undergoes an invasive and restrictive process to social conviviality [21]. With vascular alterations, the incidence of DM and SAH in dialysis allows the finding of occlusive vascular disease [11]. This, when present in the penile artery, prevents the maintenance of necessary pressures for tumescence. Regarding those comorbidities, the inflammatory process of arteriosclerosis can be found, which can also contribute to the erectile dysfunction disease.

In our study, we aim to study and evaluate hypogonadism, erectile dysfunction, and its consequences on the quality of life of CKD patients undergoing hemodialysis.

2. Material and methods

A Case-Control study was conducted with patients with CKD linked to INEFRO (Nephrology Institute, Taubaté/SP - Brazil) [6] and patients with "no CKD" accompanying for annual prostate cancer screening at a public health ambulatory. These patients were categorized into two groups, the Case group composed of chronic kidney patients already diagnosed and on hemodialysis and the Control group formed by patients under outpatient follow-up. A total of 30 patients were analyzed in each group.

The exclusion criteria of patients for both groups are: Klinefelter syndrome, testicular dysgenesis, congenital or acquired anorchia, testicular malignancy, orchitis, systemic diseases (hypothyroidism, liver diseases), Kallmann syndrome, hypogonadotropic hypogonadism already diagnosed, prolactinoma, hemochromatosis, traumas and genital infections, anabolic steroid abuse, morbid obesity, radiotherapy, senility, partial androgenic insensitivity syndrome and diabetes mellitus.

After explaining the importance of the research and signing of the Free and Informed Consent Form, in these two groups the ADAM (evaluation of the androgen disorder) and IIEF-5 were applied and the following clinical examinations were performed: orchidometry (measurement of testicular volume), analyze the distribution of hair, verify if the patient has gynecomastia and BMI analysis. For standardization of care, a clinical evaluation form was created.

After all data was collected and compiled into spreadsheets in Excel (Windows, 2007). Action Stat program (version: 3.6.331,450 build 7) was used for statistical analysis of the results. Through this platform, the Kolmogorov - Smirnov normality test was applied for the variables "age", "BMI", "orchidometry", "Presence of Systemic Arterial Hypertension (SAH)" and in the questionnaires "ADAM" and "IIEF-5" in both groups separately.

Objectives

General: To know the profile of Hypogonadism and Erectile Dysfunction in patients with chronic kidney disease on hemodialysis studied.

Specific: To question, through clinical analysis and application of ADAM and IIEF questionnaires, the consequences that these diseases trigger on the quality of life of patients on hemodialysis.

3. Results

Action Stat program (version: 3.6.331,450 build 7) was used for statistical analysis of the results. Through this platform, the Kolmogorov - Smirnov normality test was applied for the variables "age", "BMI", "orchidometry", "Presence of Systemic Arterial Hypertension (SAH)" and in the questionnaires "ADAM" and "IIEF-5" in both groups separately. The variables "BMI" and "Age" presented normal distribution, with $P > 0.005$. For these, the T-student Test was applied to compare the Case and Control groups. While the variables "Presence of SAH", "Orchidometry", "IIEF-5" and "ADAM" presented abnormal distribution with $P < 0.005$. Thus, Wilcoxon nonparametric test was applied. $P=0.002$.

3.1. Physical examination

The study sample consisted of 60 patients subdivided into two groups. As the variable Age followed normal distribution, the T-student test was applied to compare the groups with $P=0.95$.

The Case group is represented by 30 male chronic kidney patients on hemodialysis with a mean age range of 54.4 years, standard deviation of 15.14, median of 54 and mode of 76. The control group represented by 30 male patients accompanying the Urology outpatient clinic for annual prostate cancer screening, presents an age group with a mean of 54.26 years, standard deviation of 11.55, median of 53.5 and mode of 51.

Regarding the BMI of the patients, the mean case group was 24.46 kg/m² and control group 25.91 kg/m² (p= 0.089).

In the clinical evaluation, the patients of the Case group about changes in libido after the beginning of hemodialysis were questioned and for both groups the presence of Systemic Arterial Hypertension (SAH) was evaluated, the patients were confirmed about the comorbidities that constitute exclusion criteria from the study and a physical examination was performed with a focus on the presence of gynecomastia, weight and height measurement for body mass index (BMI) calculation, change in pilification and orchidometry was performed.

For patients in the Case group, 73% complained of decreased libido after initiation of hemodialysis. Of these, 41% stated that alteration occurred more than 5 years after the beginning of hemodialysis, 14% in the period of 1 to 4 years after the beginning of hemodialysis and 45% noticed a change in libido until the end of the first year of dialysis.

SAH is a comorbidity present in 77% of patients in the Case group and in 13% of patients in the Control group (p=0).

Gynecomastia was evaluated in 20% of patients in the Case group and in 7% of the Control group.

The orchimetry of the Case group revealed prevalence in 53.33% of testicular volume patients compatible with measurement 3 of the orchid meter (20 ml) (Figure 1). 10% have volume compatible with measure 1 (5 ml), 13.33% measure 2 (10 ml), 13.33% measure 4 (30 ml) and 10% correspond to measure 5 (40 ml). In the control group, the most prevalent measure was 4, found in half of the patients (50%), followed by measure 3 (33.33%), measure 5 (13.33%), measure 2 (3.33%) and no patient in the Control group presented measure 1. In the statistical analysis, p=0.002 was found.



Figure 1 Photograph of the orchidometer used in the study

3.2. ADAM

Patients were asked to answer the ADAM questionnaire by marking as an option a "yes" or "no" for each of the questions, based on the last four months. Patients who did not practice physical activity were instructed to mark that they did not present a reduction in sports activities.

The mean ADAM score for patients in the Case group was 4.2 points and the Control group was 1.9 points (p=8.00E-0.4).

The results of the ADAM questionnaire applied to patients in the Case group revealed that 60% have observed a decrease in libido, 63.33% have lacked energy, 63.33% perceived a reduction in muscle strength, 23.33% perceived height loss, 30% perceived mood changes frequently, 70% perceived that the erections are less vigorous, 53.33% reduced sports activities, 26.66% felt drowsiness after dinner and 30% reported worsening in professional performance. When evaluated with respect to the ADAM questionnaire score, two patients presented 0 (zero) points, four patients had 1 (one) point, one patient obtained 2 (two) points, five patients obtained 3 (three) points, five patients obtained 4 (four) points, five patients had 5 (five) points, six patients scored 6 (six) points, one patient obtained 7 (seven) points, four patients obtained 8 points and no patient had nine or ten points.

The results of the Control group in the ADAM questionnaire showed that 30% have observed decreased libido, 16.66% had a lack of energy, 23.33% perceived a reduction in muscle strength, 10% perceived a loss of height, 13.33% perceived mood changes frequently, 30% perceived that the infections are less vigorous, 10% reduced sports activities, 30% felt drowsiness after dinner and 33.33% reported worsening in professional performance.

The prevalence of affirmative answers to the questions in the ADAM questionnaire is expressed in the comparative table below (Table 1).

Table 1 Prevalence of affirmative answers to ADAM questionnaire questions in both groups

Prevalence of affirmative answers to ADAM questionnaire questions in both groups		
	Case	Control
Do you have you a decrease in libido?	60%	30%
Do you have you a lack of energy?	63,33%	16,66%
Do you have a decrease in strength and/or endurance?	63;33%	23,33%
Have you lost height?	23,33%	10%
Are you sad or grumpy often?	30%	13,33%
Are your erections less strong?	70%	30%
Have you noticed a recent deterioration in ability to play sports?	53;33%	10%
Are you fallen asleep after dinner?	26,66%	30%
Has there been a recent deterioration in your work performance?	30%	33;33%

Of these, eleven patients obtained 0 (zero) points in the questionnaire, six patients obtained 1 (one) point, three patients obtained 2 (two) points, two patients obtained 3 (three) points, four patients had 4 (four) points, three patients had 6 points, one patient obtained 7 points. No patient scored 5, 8 and 9 points.

The ADAM questionnaire score of the Case and Control groups can be better expressed in Graphic 1.

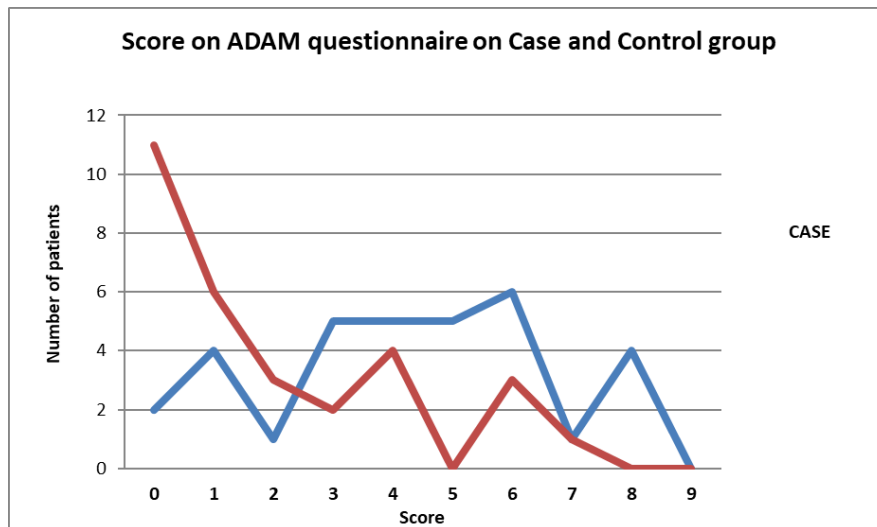


Figure 1 Score of patients from the Case and Control groups in the ADAM questionnaire

Among the questions that indicate symptoms corresponding to late male hypogonadism, when there is the presence of symptoms of sexual dysfunction, the clinical suspicion of ADAM is increased. Sexual disorders are best investigated by questions: "Do you have you a decrease in libido?" and "Are your erections less strong?". In the analysis of the results 60% of patients in the Case group revealed a decrease in libido while in the Control group the incidence decreased by half (30%), results expressed in graphic 2.

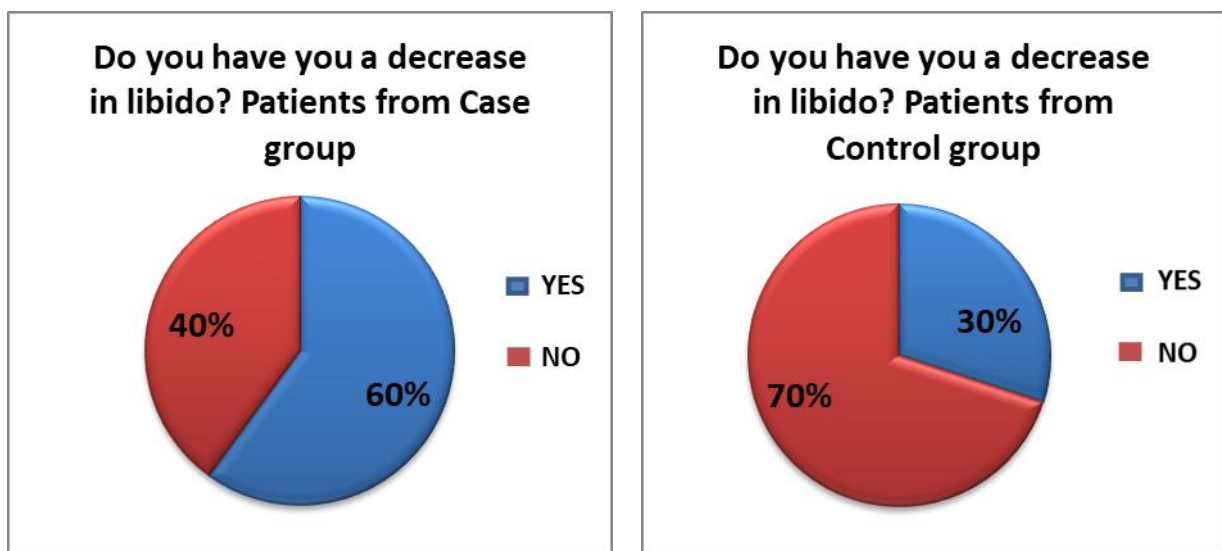


Figure 2 Patient results from the Case (left) and Control (right) groups for the question " Do you have you a decrease in libido?"

Regarding "Are your erections less strong?", in the Case group 70% they perceived that the erections are less vigorous and in the control group 30% (graphic 3).

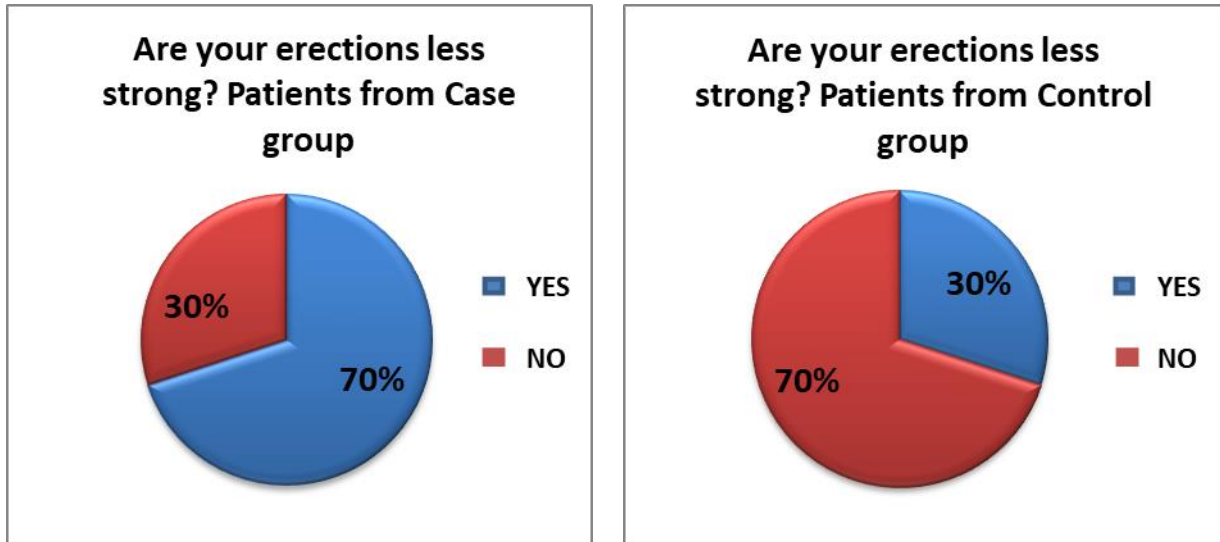


Figure 3 Patient results from the Case (left) and Control (right) groups for the question "Are your erections less strong?"

At the intersection of data in the Case group, 69.56% of patients present both decreased libido and less vigorous erections, 8.7% presented decreased libido (alone) and 21.73% less vigorous (isolated) erections.

3.3. IIEF-5

In the analysis of the International Erectile Function Index - 5, the mean score of the Case group was 16.63 and the Control 19.93 ($p=0.045$).

60% of patients in the Case group and 50% of the Control group have some degree of Erectile Dysfunction (ED). When stratified the degree of ED, in the Case group 10% presents mild dysfunction, 23% mild to moderate, 17% moderate and 10% severe. In the Control group, mild ED increases to 27%, mild to moderate ED decreases to 13% of patients, moderate ED corresponds to 7% and severe ED represents 3% of patients (Graphic 4).

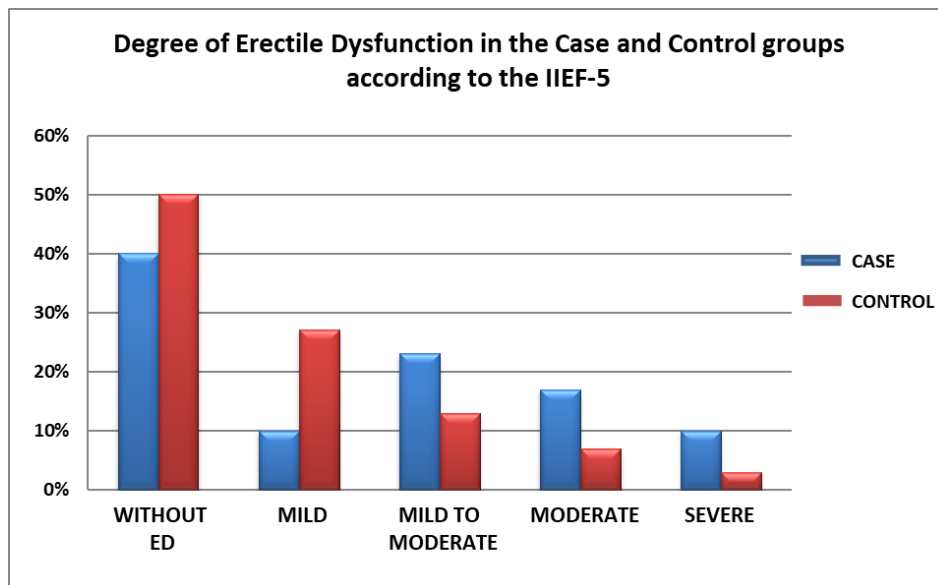


Figure 4 Degree of Erectile Dysfunction in the Case and Control groups according to the IIEF-5 questionnaire

Table 2 Result as a percentage of the Case and Control groups for each alternative of the questions in the IIEF-5 questionnaire

Results of the answers to the IIEF-5 questionnaire in the Case and Control groups		
	Case	Control
How do you rate your confidence that you could get and keep an erection?		
Very low 1	26;60%	0%
Low 2	16;60%	13;33%
Moderate 3	23;30%	30%
High 4	13;30%	16;66%
Very high 5	20%	40%
When you had erections with sexual stimulation, how often were your erections hard enough for penetration?		
Almost never / Never 1	13;33%	6;66%
A few times (much less than half the time) 2	23;33%	6;66%
Sometimes (About half the time) 3	10%	20%
Most times (much more than half the time) 4	13;30%	10%
Almost always / Always 5	40%	56;66%
During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?		
Almost never / Never 1	20%	13;33%
A few times (much less than half the time) 2	16;60%	3;33%
Sometimes (About half the time) 3	13;33%	26;66%
Most times (much more than half the time) 4	13;33%	6;66%
Almost always / Always 5	36;60%	50%
During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?		
Extremely Difficult 1	26;60%	6;66%
Very Difficult 2	6;60%	6;66%
Difficult 3	16;60%	3;33%
Slightly Difficult 4	13;30%	16;60%
Not difficult 5	36;60%	60%
When you attempted sexual intercourse, how often was it satisfactory for you?		
Almost never / Never 1	13;33%	3;33%
A few times (much less than half the time) 2	10%	10%
Sometimes (About half the time) 3	13;30%	13;33%
Most times (much more than half the time) 4	10%	16;66%
Almost always / Always 5	53;33%	56;66%

In question "How do you rate your confidence that you could get and keep an erection?" in the Case group 26.6% are not confident or have very low confidence, 16.6% low confidence, 23.3% moderate, 13.3% high and 20% very high degree of confidence. In the Control group, in turn, no patient was not confident or very unconfident in being able to have and maintain the ordination, 13.33% had low confidence, 30% moderate, 16.66% high and 40% very high confidence.

When asked about erections rigid enough to achieve penetration, question: "When you had erections with sexual stimulation, how often were your erections hard enough for penetration?", in the Case 13.33% group revealed that they never or almost never manage to penetrate sexual intercourse, 23.33% achieve a few times (less than half), 10% achieve half of the time, 13.3% often (more than half) and 40% almost always or always achieve penetration with erect penis. The same question for patients in the Control group found that more than half (56.66) almost always or always get sufficient for penetration and 6.66% answered the option "almost never or never".

Question "During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?" infers about remaining with penile erection after penetration. In the case group, 36.6% almost always or always manage to remain with erect penises, "many times (more than half)" and "sometimes (about half)" was answered by 13.33% in each of the options, 16.6% infer a few times (less than half) and 20% never manage to remain. Different results were evidenced in the Control group, in which half of the interviewed patients (50%) were able to remain with the penis erect after penetration, 26.66% about half of the time and 3.33% a few times (less than half). The option "many times (more than half)" and "almost never/never" presented incidence of 6.66% and 13.33%, respectively.

In the following question, "During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?" authors wondered about being able to maintain the penile erection until the end of sexual intercourse. In the Case group it was not difficult for 36.6% of the patients, while 26.60% reported that it was extremely difficult. For 13.3% it is slightly difficult, 16.6% is difficult and 6.6% answered it was very difficult. In the Control group, more than half (60%) manage to maintain the erection rate until the end of the sexual act, while for 16.6% the task is slightly difficult, for 3.3% it is difficult, and the "very difficult" and "extremely difficult" options were chosen by 6.66% of the patients in each of the options.

Question "When you attempted sexual intercourse, how often was it satisfactory for you?", reflects high satisfaction for 53.33% of patients in the Case group, 10% answered that more than half of the time they felt satisfied, 13.3% sometimes, 10% a few times (less than half) and dissatisfaction in 13.33% of patients. The degree of dissatisfaction decreases to 3.33% in the Control group, in addition to 10% of patients presenting few times, 13.33% sometimes, 16.66% many times and high satisfaction was present in 56.66% of the interviewees of this group.

4. Discussions

According to data from the 2017 Dialysis Census published by the Brazilian Society of Nephrology [6], the number of dialysis patients in Brazil almost tripled in the period from 2000 to 2017, from 42,695 to 126,583 Brazilians, with a prevalence of 58% male and aged 45 to 64 years (42.6%). As expected, course of CKD, patients who reach stage 5, known as the "phase of chronic kidney disease" with glomerular filtration rate lower than 15 ml/min, experience the lack of control of metabolic and endocrine functions, generating a uremic environment, which is related to hypogonadism and erectile dysfunction, because of the imbalance of the hypothalamus-pituitary axis. [7].

In parallel, it is known that men from 40 years of age experience a drop in serum testosterone levels, about 0.4 to 2% per year [12], which corroborates the appearance of signs and symptoms such as decreased libido and erectile dysfunction, decreased muscle mass, increased adipose tissue and fat redistribution, decreased bone density, mood changes and psychological imbalance and decreased testicular volume [22], characterizing the Androgenic Disorder of Aging Male (ADAM).

To facilitate the screening of clinical evaluation of these patients, Morley [23] proposed the ADAM questionnaire from St Louis University, with sensitivity of 88% and specificity of 60% to detect hormonal deficiency in men with low bioavailable testosterone (<71ng/dL). Years later in a second study, a sensitivity of 97% and specificity of 30% were found. The questionnaire addresses questions for screening for decreased libido, lack of energy, reduced muscle strength, mood impairment, impaired injuries, loss of vitality for sports activities, drowsiness after dinner and worsening of professional performance. These criteria clinically characterize EMD [23]. Positivity for the questionnaire occurs when questions involving changes in libido or loss of quality of erections are positive or at least three other questions in which the patient answered "YES" [24].

In addition to the validation performed by St. Louis University, the ADAM questionnaire was applied in different populations, with paired hormonal dosage in order to predict how specific and sensitive its use is in the screening of Hypogonadism. Martinez-Jabaloyas, [24] conducted a prospective study in Spain with 230 men over 50 years (mean age 66.3 years), with or without associated underlying diseases and/or minimal urological pathologies and found positivity in the ADAM questionnaire in 67.9% of them [24]. Nearby value was found by Cabral [25], who obtained 70.8% positivity in the ADAM questionnaire when evaluating 460 men over 40 years of age (mean age of 57.17 years), without chronic diseases that could interfere with testosterone levels, without alcohol or drug abuse and without diagnosis of prostate cancer, who participated in a prostate cancer screening program at the Hospital das Clínicas de Porto Alegre [25].

In the present study with men with a mean age of 54.4 years in the Case group and 54.26 years in the Control group, it was observed that 80% of the patients in the first group were positive for the ADAM questionnaire against 33% of positivity in the second group.

Sexual disorders, expected in patients with hypogonadism, are explored in the ADAM questionnaire. In analyzing the question "Are your erections less strong?" in the Case group 70% answered "YES" to the item, being the question with the highest percentage of affirmative answer in this group. Such evidence was also found by Morley [23]. who presented for this same question the highest positivity rate (60.8%) in relation to the other questions. In the same study, Morley [23] found positivity for a question about loss of libido in 48.1% of the interviewees, a value lower than the current study (60%). As the ADAM questionnaire presented a prediction sensitivity for hypogonadism of 97% by this same author, we can infer that our patients present some degree of this condition, but to confirm this diagnosis testosterone should be dosed, which was not possible in the present study [26].

The ED defined by the NIH Consensus Statement (1992) as a persistent difficulty in obtaining and/or maintaining a sufficient erection for satisfactory sexual performance [18] has an important worldwide prevalence. According to projection of A.A. AYTAÇ et al. in 2025 around 322 million people will present the disorder [27]. Due to factors such as gonadal, neuropathic, and vascular dysfunction, anemia, associated comorbidities, as well as psychological influence and interpersonal impact, patients in the final stage of CKD represent an important part of this group.

Several studies have used the International Index of Erectile Function (IIEF), validated [28] and adapted for use in Portuguese [29] as an instrument for measuring erectile function. The questionnaire consists of 15 questions that assess 5 dimensions: erectile function, orgasmic function, sexual desire, sexual intercourse satisfaction and overall sexual satisfaction. For each chosen answer option, a score is generated. The final score is the result of the sum of the scores of all questions. In this work we used the simplified version IIEF-5, classifying as Absence of ED (22-25 points), Mild (17 to 21 points), Mild to Moderate (12 to 16 points), Moderate (8 to 11 points) and Severe (5 to 7 points) [30].

Through the application of the IIEF-5 questionnaire, the present study found in the group of patients with CKD on hemodialysis prevalence of ED in more than half of the sample analyzed (60%), data that agrees with other studies that demonstrate that the prevalence can reach and exceed 70% to 80% of these patients [31]. Sankar D. Navaneethan in a meta-analysis conducted with 21 studies and 4389 patients found some degree of ED in 70% of them [32]. Antonucci M showed a similar prevalence of 71% in a study that compared ED in hemodialysis patients and patients undergoing kidney transplantation [33]. According to Costa M 81.1% of chronic kidney patients grades 4 or 5 had some level of ED, using the questionnaire and hormonal dosage [34].

The second applicability of the IIEF-5 questionnaire is the stratification of ED. The current study revealed that of the 60% of patients in the Case group who presented ED, 23% were Mild to Moderate, followed by Moderate (17%). Similar results were seen by Santos P R in which the application of the IIEF-5 questionnaire stratified that most of the 42% of patients with ED were mild (20.3%) [16].

In the individual analysis of question 5 on satisfaction after sexual intercourse, we obtained that 63.33% of patients in the Case group are satisfied many times, almost always or always. In a sample in which 36.66% of CKD patients never, almost never or rarely get enough of an erection for penetration (question 2) and almost half of them (49.8%) consider it difficult, very difficult or extremely difficult to maintain an erection until the end of sexual intercourse (question 4), the high rate of satisfaction after sexual intercourse (question 5) seems to be incongruous. It is necessary to consider that these patients after the beginning of hemodialysis undergo changes in daily life, physical and social limitations, sometimes suffer emotional destructuring and even can resignify the ideal of sexual satisfaction. Moreover, as already mentioned, age is a significant factor that explains erection disorder. In this study, the mean age was 54.4 years (SD 15.14) and predominant age group above forty years (86%), age at which man begins to experience the declines of serum testosterone and its manifestations (DAEM). Age also goes through the psychological sieve about how middle-

aged men analyze satisfaction in a relationship. This theme was the object of study by MARREGA, M F in his thesis on being a man of 45 to 55 years of age in a heterosexual relationship. As observed in one of the middle-aged interviewees, the incessant search for adventure, sexual pleasure and self-affirmation of youth begin to coexist with the need for the complicity of a partner [35].

The analysis of results in a population of chronic patients with systemic manifestations requires discussion of variables when studying erectile dysfunction. Age is pointed out in several studies [31;11;19;36;34] as a factor that influences the dynamics of penile erection because it is related to hypogonadism. Considering that the mean age in the groups was similar (in case 54.4 ± 15.14 and in the control 54.2 ± 11.75), it does not seem to impact the data. In addition, associated with senility, these patients usually present other comorbidities such as DM and SAH.

Among the aforementioned comorbidities, diabetic nephropathy is pointed out as the main cause of terminal CKD in the world [37,19]. It is mainly responsible for endothelial dysfunctions and was considered an exclusion criterion in this study. SAH, the first cause in Brazil of ED in CKD was considered in the study, as it is presented by most dialysis patients and if it were considered an exclusion criterion, the population analyzed would represent an insignificant portion of the sample of patients from the Dialysis Institute. In addition, it is in the interest of the work to analyze its prevalence in the population of the Case group. This impact of this comorbidity is remarkable when analyzing the prevalence in the groups, while 77% of chronic renal patients on hemodialysis are hypertensive, in the Control group 13%. At the same time, SAH is a criterion of impact on the analyzed data since the groups are not homogeneous in these criteria.

Obesity is one of the signs present in hypogonadism that can be attended with ED [22]. It is pointed out that the Body Mass Index (BMI) has an inverse relationship with testosterone levels, so obesity would be related to decreased production of the hormone [25]. This impact can even be demonstrated in the 2nd Brazilian Consensus of ED (2002), in which it was expressed that the lipid profile is among the laboratory tests of minimum evaluation of the pathology [38]. In view of this, the BMI of the patients studied with homogeneous means in the groups (24.4 in the Case and 25.9 in the Control) was analyzed, but in different classifications. Hemodialysis patients have strict weight control and a balanced diet, which may justify the average compatible with normality (eutrophic), while the participants of the Control group on average are overweight. However, despite different classifications, the proximity of the means does not seem to be an interference factor in the comparison of groups when causing ED. The deposition of adipose tissue in the male breast (gynecomastia) was also analyzed in the Case population, with a prevalence of 20% and in the control 7%.

Orchidometry was performed in patients since hypogonadism may occur with structural alterations such as disarrangement of seminiferous tubules, interstitial fibrosis, and areas of calcification, which lead to decreased testicular volume [39]. Group Case 76.6% had a classification lower than or equal to TG3 (20 ml) while in the control 96.66% have testicular volume larger than or equal to TG3. Body pilification alteration was found in 33% of patients after hemodialysis initiation, a common sign in hypogonadal patients.

Regarding the impact of hemodialysis on libido, 73% of patients reported decreased sexual desire after the beginning of dialysis.

Considering that the patients presented reduction of testicular volume, gynecomastia, decreased libido after dialysis when compared to the Control group, we can infer that these patients present some degree of hypogonadism causing ED. One of the limitations of the study is the lack of laboratory testosterone dosage, necessary for diagnostic confirmation of hypogonadism when associated with the patient's clinic [12].

Abbreviations

- ADAM: Androgenic Deficiency in the Aging Males
- ED: Erectile Dysfunction
- CKD: Chronic Kidney Disease
- DM: Diabetes Mellitus
- FSH: Follicle stimulating hormone
- SAH: Systemic Arterial Hypertension
- IIEF: International Index of Erectile Function
- BMI: Body mass index
- LH: Luteinizing Hormone
- GnRH: Gonadotropin hormone stimulator

5. Conclusions

The present study aimed to analyze hypogonadism and ED in patients with CKD undergoing kidney replacement therapy. It can be inferred that patients in the Case group experience early, throughout the dialysis process, a direct impact on sexual quality, with decreased libido and difficulty in the reaction when compared to the Control group. The limitations that hemodialysis imposes reflect on a psychosocial impact, an important factor of ED, which corroborates the differences between the groups. Comorbidities, such as SAH, prevalent in 77% of patients in the Case group also act as a predisposing factor.

The expected androgenic disorder in men from the age of 40 years (ADAM) and changes in the hormonal axis caused by uremia were indicated by the questionnaires but could not be differentiated and confirmed in this study due to the lack of laboratory dosage of total testosterone, prolactin and gonadotropins.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

Statement of ethical approval

This study was submitted to the Ethics Committee on Human Research of the University of Taubaté (UNITAU) and accepted through the Brazil Platform (No. 2011978).

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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