

Prevalence of Sexual and Gonadal Dysfunctions in Male Patients on Regular Hemodialysis: A Cross-Sectional Study

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Abstract:

Background: Despite the significance of these concerns, dialysis patients' follow-up care marginalizes sexual dysfunction (SD), and physicians' attention given to this problem remains scant.

Aim and Objectives: To investigate the prevalence of gonadal dysfunction and sexual dysfunction in male hemodialysis patients (18–60 years old; sexually active males) and how it relates to serum prolactin, free testosterone level, and semen analysis in Assiut University Hospitals.

Patients and Methods: All male patients with ESRD on chronic HD who were treated at the Assiut University Hospitals' Nephrology and Hemodialysis Unit, Internal Medicine Department, between November 2020 and November 2021. This was an observational cross-sectional study. There were 150 male patients in hemodialysis units overall; however, only 56 of them were included in this study, and the rest of them were excluded due to comorbidities such as DM, HTN, and cardiac diseases, which may affect the results.

Results: All patients showed decreased libido, and 71.4% of them had erectile dysfunction after starting HD. The IIEF score indicates a marked decline in sexual desire, erectile function, orgasmic function, and satisfaction during intercourse, and overall satisfaction. Semen analysis results showed reduced volume, total count, concentration, vitality, and total motility, presenting evidence that uremia affects spermatogenesis and total sperm quality, which consequently causes adverse effects on patient fertility.

Conclusion: Erectile dysfunction (ED) prevalence is very high among HD patients; the most common cause is an endocrinological disturbance that is mainly caused by uremia, leading to increased prolactin and a low testosterone level. Also, hormonal disturbances and uremia affect semen quality, which subsequently affects patient fertility.

Keywords: *Sexual and Gonadal dysfunctions; Regular Hemodialysis; Cross-Sectional Study.*

Introduction:

Male patients with End Stage Renal Disease (ESRD) may experience reduced libido, erectile dysfunction, premature or

delayed ejaculation, and altered spermatogenesis as symptoms of gonadal dysfunction.^[1] Men with ESRD receiving continuous hemodialysis frequently have

gonadal dysfunction, and erectile dysfunction is one of the most prevalent signs of sexual dysfunction, with up to 70% of hemodialysis patients reporting having it. [2-4]

The problem is multifactorial. [5] The most significant contributing factor is testosterone insufficiency and deficit, which are common findings in male hemodialysis patients (66% and 24%, respectively). [6]

Usually, total and free testosterone levels are lowered [7]. Increased serum Gonadotropin concentrations typically follow it due to disruption of the hypothalamic-pituitary-gonadal axis (uremic hypogonadism). [8]

changes in the pulsatile release of gonadotropin-releasing hormone (GnRH), which results in uremia from insufficient dietary intake, stress, and systemic disease, and causes a hypogonadal condition for the patient. [9,10]

Since testosterone typically acts as a feedback inhibitor of LH release, it is believed that decreased testosterone release from the Leydig cells is the source of excess luteinizing hormone (LH) secretion. In men with chronic kidney failure, follicle-stimulating hormone (FSH) secretion is likewise elevated, and the metabolic clearance rate of LH is decreased due to decreased kidney clearance. [11]

Extreme hyperprolactinemia has been linked to infertility, loss of libido, and low circulating testosterone levels; therefore, owing to testosterone deficiency and hyperprolactinemia at ESRD as one of the most important factors and exclusion of other factors, elevated plasma prolactin levels are frequently found in men receiving hemodialysis [12] Men receiving long-term hemodialysis exhibit varying degrees of infertility or subfertility as a result of decreased spermatogenesis, testicular injury, and erectile dysfunction. [13]

The goal of the study was to investigate the prevalence of gonadal dysfunction and its

relationship to serum prolactin, free testosterone, and semen analysis in male hemodialysis patients (HD) aged 18–60 years (sexually active males) in Assiut University Hospitals.

Patients and Methods

All male patients with ESRD receiving chronic hemodialysis in Assiut University Hospitals' Nephrology and Hemodialysis Unit, Internal Medicine Department, from November 2020 to November 2021, were included in this observational cross-sectional study. Out of the 150 male patients in hemodialysis units, only 56 were included in this study. The remaining patients were eliminated because they had comorbid conditions such as diabetes, hypertension, and cardiac disorders, which could have an impact on the results.

The proportion of adult males with gonadal dysfunction who are between the ages of 18 and 60 who receive regular hemodialysis in most previous studies was 30-80%. So we hypothesized that 50% of adult males between the ages of 18 and 60 who were receiving regular hemodialysis had gonadal dysfunction. We used EPI-Info 7 to calculate the sample size. Based on this percentage, and with confidence levels of 80% and 10%, the minimum sample size required for the study was estimated to be 41 patients.

Methodology:

Full history taking includes:

Name. Age, marital status, and occupation, other comorbidities as diabetes, hypertension, heart failure, etc., offspring before hemodialysis, conception problems before and after hemodialysis, and history of genital surgery, trauma, and/or irradiation.

Full Clinical examination:

Vital signs and anthropometric measures (weight and height for BMI calculation) are part of a general examination. A comprehensive neurological, abdominal, cardiac, and chest examination was conducted to identify risk factors.

Study Tools:

The following scales are used to evaluate each patient included: Arabic version of the International Index of Erectile Function

(IIEF) Questionnaire's erectile function score. [14,15]

INTERNATIONAL INDEX OF ERECTILE FUNCTION
 Patient Questionnaire

HOSPITAL NUMBER (IF KNOWN)
 NAME
 DATE OF BIRTH AGE
 ADDRESS
 TELEPHONE

These questions ask about the effects that your erection problems have had on your sex life over the last four weeks. Please try to answer the questions as honestly and as clearly as you are able. Your answers will help your doctor to choose the most effective treatment suited to your condition. In answering the questions, the following definitions apply:

- sexual activity includes intercourse, caressing, foreplay & masturbation
- sexual intercourse is defined as sexual penetration of your partner
- sexual stimulation includes situation such as foreplay, erotic pictures etc.
- ejaculation is the ejection of semen from the penis (or the feeling of this)
- orgasm is the fulfilment or climax following sexual stimulation or intercourse

OVER THE PAST 4 WEEKS
CHECK ONE BOX ONLY

When you have sexual stimulation, how often are you aroused hard enough for intercourse?	0 No sexual activity 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always	<input type="checkbox"/> Q1	
When you attempt intercourse, how often are you able to (enter) your partner?	0 Did not attempt intercourse 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always	<input type="checkbox"/> Q2	When you have often were you penetration?
When you attempt intercourse, how often are you able to maintain erection after you had penetrated your partner?	0 Did not attempt intercourse 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always	<input type="checkbox"/> Q3	When you are able to penetrate?
		<input type="checkbox"/> Q4	During sexual intercourse (entered) you

<input type="checkbox"/> Q6	How many times have you attempted sexual intercourse?	0 No attempts 1 One to two attempts 2 Three to four attempts 3 Five to six attempts 4 Seven to ten attempts 5 Eleven or more attempts
<input type="checkbox"/> Q7	When you attempted sexual intercourse, how often was it satisfactory for you?	0 Did not attempt intercourse 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
<input type="checkbox"/> Q8	How much have you enjoyed sexual intercourse?	0 No intercourse 1 No enjoyment at all 2 Not very enjoyable 3 Fairly enjoyable 4 Highly enjoyable 5 Very highly enjoyable
<input type="checkbox"/> Q9	When you had sexual stimulation or intercourse, how often did you ejaculate?	0 No sexual stimulation or intercourse 1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
<input type="checkbox"/> Q10	When you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?	1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
<input type="checkbox"/> Q11	How often have you felt sexual desire?	1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always

<input type="checkbox"/> Q10	When you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?	1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
<input type="checkbox"/> Q11	How often have you felt sexual desire?	1 Almost never or never 2 A few times (less than half the time) 3 Sometimes (about half the time) 4 Most times (more than half the time) 5 Almost always or always
<input type="checkbox"/> Q12	How would you rate your level of sexual desire?	1 Very low or none at all 2 Low 3 Moderate 4 High 5 Very high
<input type="checkbox"/> Q13	How satisfied have you been with your <u>overall sex life</u> ?	1 Very dissatisfied 2 Moderately dissatisfied 3 Equally satisfied & dissatisfied 4 Moderately satisfied 5 Very satisfied
<input type="checkbox"/> Q14	How satisfied have you been with your <u>sexual relationship</u> with your partner?	1 Very dissatisfied 2 Moderately dissatisfied 3 Equally satisfied & dissatisfied 4 Moderately satisfied 5 Very satisfied
<input type="checkbox"/> Q15	How do you rate your <u>confidence</u> that you could get and keep an erection?	1 Very low 2 Low 3 Moderate 4 High 5 Very high

Figure (1): The International Index of Erectile Function (IIEF) Questionnaire's erectile function score.

Laboratory Investigations:

Represented by, complete blood count, random blood sugar and HbA1c, kidney function tests (serum urea & creatinine) with calculation of estimated glomerular Filtration Rate[15] (The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to compute the GFR.), coagulation profile (Prothrombin Time-Prothrombin Concentration-international normalization Ratio-APTT), serology including HBV, HCV, HIV and semen analysis (by masturbation) ended finally by free testosterone level at 8-10 am and Prolactin levels (ELISA method).

Statistical Analysis:

Version 22 of SPSS (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) was used for all statistical computations. The statistical descriptions of the data were mean \pm standard deviation (\pm SD), or when the data were not normally distributed, median and Interquartile Range (IQR), frequencies (number of instances), and relative frequencies (percentages), if

appropriate. Since the data were not normally distributed, the Kruskal-Wallis test was used to compare the quantitative variables. Mann-Whitney, when comparing binomial data over time, employed the U test. Chi-square (χ^2) test was used to compare categorical data. When the expected frequency is less than five, an exact test was utilized in its place. The Spearman's rho correlation test was used to determine the correlation between different variables. A two-tailed P-value is considered significant when the level is less than 0.05.

Ethical Considerations:

IRB; Assiut Faculty of Medicine approved the methodology and the study design (IRB number is 17101337). The research volunteers gave their signed informed consent before beginning the study. The entire study was conducted confidentially. The study's subjects were not exposed to any risks, and whether or not they participated in the study had no bearing on the quality of the healthcare they received.

Results

Table (1): Basic demographic data and laboratory investigations.

Variables	Mean \pm SD*	Median
Age in years	33.929 \pm 7.7409	33.500
Duration in years	7.000 \pm 4.9138	5.000
Weight in kgs	77.3929 \pm 8.44808	78.0000

Height in cm	170.9286±7.49753	175.5000
BMI*	25.0464±2.72917	24.9000
Hemoglobin level in g/dl	11.11±.4060	11.00
Creatinine level in µmol/L	560.8571±184.30562	742.5000
Urea in mmol/L	25.9643±9.88840	34.5000

*SD standard deviation. *BMI: body mass index. *The normal serum creatinine (^sCr) =53 to 106 µmol/L.^[16] *The normal range of urea nitrogen =1.8 to 7.1 mmol urea per liter

Forty-four patients (78.6%) out of 56 were married and 12 (21.4%) were single, with a mean age=33.9±7.7 years. Fertility and intercourse satisfaction can only be assessed in married patients, not in singles, due to the

religious and cultural background in our community. Four patients out of 56 have no ejaculation at all, so that semen analysis can be assessed only in 52 patients out of the total number.

Table (2): Gonadal function before HD.

	Frequency (no.)	Percentage (%)
Decrease libido		
Yes	0	0
No	56	100
Erectile dysfunction		
Yes	0	0
No	56	100
Infertility (n=44 only married)		
Yes	0	0
No (fertile)*	44	100
Presence of Ejaculation		
Yes	56	100
No	0	0

* Single male patients are excluded

GD was assessed before HD and showed that 100% of patients didn't show any of decreased libido, erectile dysfunction,

infertility (which can only be assessed in married individuals), or absence of ejaculation.

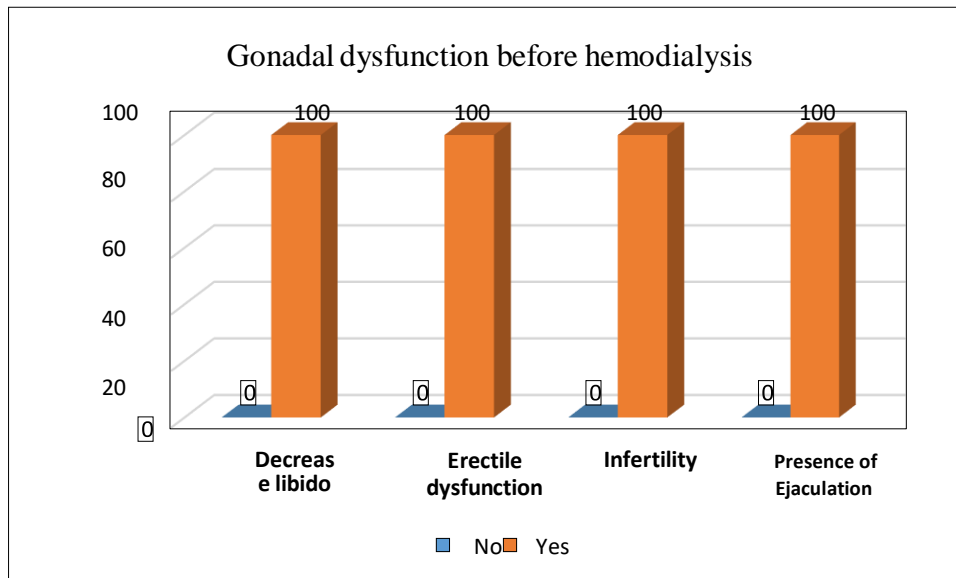


Figure (2): GD before HD of study participants (n=56).

Table (3): Gonadal dysfunction after HD of study participants (n=56).

	Frequency (no.)	Percentage (%)
Decrease libido		
Yes	56	100
No	0	0
Erectile dysfunction		
Yes	40	71.4
No	16	28.6
Infertility (n=44)		
Yes	37	84.1
No (fertile)	7	15.9
Presence of Ejaculation		
Yes	52	92.9
No	4	7.1

Gonadal dysfunction was also assessed after hemodialysis; 56 (100%) showed decreased libido, and 71.4% of them had erectile dysfunction, 84.1% were infertile,

and 92.9% had ejaculation. And there is an obvious gonadal dysfunction after starting HD.

Table (4): Study participants' International Index of Erectile Function (IIEF) scores (n = 56).

	(Mean±SD)	Median, IQR
A-Erectile function	17.6±6.09	19.00,11.0
B-Orgasmic function	5.85±2.3	6.5,4.0

C-Sexual desire	5.18±2.01	5.00,2.75
D-Intercourse satisfactory	7.04±3.27	7.5,5.00
E-Overall satisfaction	5.07±2.1	5.00,2.75

Domain maximum scores in the IIEF score. **A. Erectile Function** =30 (impaired ED if score < 26) (1). **B. Orgasmic Function**=10. **C. Sexual Desire**=10. **D. Intercourse Satisfaction** =15. **E. Overall Satisfaction** =10

The 15 questions in the validated, multidimensional, self-administered IIEF questionnaire cover the four primary domains of male sexual function (erectile function, orgasmic function, sexual desire, and intercourse satisfaction). The questionnaire has been found useful in

clinical settings. The IIEF score was calculated using the following as the mean. 17.6±6.09 was the erectile function, 5.85±2.3 was the orgasmic function, 5.18±2.01 was the sexual desire, 7.04±3.27 was the satisfactory intercourse, and 5.07±2 was the overall satisfactory performance.

Table (5): Laboratory results of free testosterone and prolactin of study participants (n=56).

	(Mean ±SD)	Median, IQR
Free testosterone level (pg/ml)	32.14±25.4	21.00, 30.42
Serum prolactin level (ng/ml)	24.28±6.21	23.5, 7.4
	Frequency (no.)	Percentage (%)
Free testosterone level (pg/ml)		
Normal level (66-309pg\ml)	12	21.4
Low level	44	78.6
Serum prolactin level (ng/ml)		
Normal level (less than 20 ng\ml)	10	17.8
Higher level	46	82.2

The mean free testosterone level was 32.14±25.4 pg/ml, normal range of free testosterone level=66-309pg\ml^[17]. In our results, 12 (21.4 %) have a normal free testosterone level, and 44 (78.6%) have a low level below the lower limit of the normal range.

The prolactin level in serum was 24.28±6.21 ng/ml on average. For boys and adult males, the typical ranges for prolactin are 3–18 ng/ml. The threshold of 20 ng/mL is regarded as hyperprolactinemia ^[18], serum prolactin above the normal limit in 46

(82.8%), and within normal range in 10 (17.8%).

Discussion

In this study, eight of the total number who had ejaculation with azoospermia (no sperm were detected) were married and had children before starting dialysis. It suggests that these eight patients' reproductive health and semen quality were normal before their uremia, and that their azoospermia developed after starting dialysis, as previously documented. ^[13,19]

Serum free testosterone, the active, unbound portion of total testosterone that

makes up 0.5-2 percent of total testosterone, was measured in this study. Total testosterone measurement is deemed sufficient unless there is a notable disruption in the synthesis of albumin and sex hormone binding globulin (SHBG). Nonetheless, in individuals with end-stage renal disease (ESRD), the level of circulating SHBG may fluctuate due to many factors; hence, the most reliable indicator is free testosterone.^[20]

In this study, the mean free testosterone level was 32.14 ± 25.4 pg/ml, which is markedly decreased from the normal average in adults (66-309 pg/ml) (2). SO, 21.4 % had normal free testosterone level, and 78.6% had testosterone deficiency, and this result is similar to a previous related study.^[21,22]

The uremic affection of the hypothalamic-pituitary-testicular axis, luteinizing hormone (LH), follicle-stimulating hormone (FSH) accumulation, reduced GnRH secretion, elevated serum prolactin (PRL), and decreased 5- α reductase activity (enzyme that converts testosterone to its active metabolite dihydrotestosterone DHT) are the causes of low testosterone concentration in men receiving hemodialysis.^[23]

Regarding the results of this study, testosterone deficiency had a significant correlation with sexual dysfunction in the IIEF questionnaire, as erectile dysfunction, orgasmic function, and decreased sexual desire; p-values were 0.044, 0.014, and 0.035, respectively; those results are similar to previous studies.^[24]

According to the current study, the mean blood prolactin level was 24.28 ± 6.21 ng/ml, which indicates that 82.8% of patients had hyperprolactinemia and 17.8% had levels within the normal range. The proportion ranges from 30% to 65% as reported in the findings of earlier investigations on hyperprolactinemia. This might result from the different sample sizes

and stringent exclusion standards applied in the current investigation, which reduced the number of patients in the sample.^[25,26]

The current study found a significant negative correlation (p-values of 0.019, 0.024, 0.044, and 0.001) between serum prolactin level and erectile function, orgasmic function, sexual desire, and overall satisfaction in the IIEF score. This suggests that raising prolactin levels affects patient fertility. These findings are consistent with earlier research ^[27,28,12]. In addition to impairing a patient's ability to conceive, elevated prolactin levels can lead to insulin resistance, metabolic syndrome, inflammatory regulation, endothelial dysfunction, atherosclerosis, elevated LDL cholesterol, triglycerides, and a higher risk of cardiovascular death in individuals with chronic kidney disease.^[25,26]

Furthermore, a noteworthy association was observed between the length of HD and the prevalence and severity of ED. These findings are consistent with those of other earlier research that discovered that beginning HD significantly reduced the frequency of sexual encounters, desire, erectile dysfunction, and the ability to experience an orgasm during sexual engagement^[29,30]

This study demonstrated a strong association between the length of HD treatment and the quality, concentration, total count, and motility of sperm. This correlation can be explained by the fact that HD therapy cannot cure all metabolic problems, replace renal endocrine function, or eliminate uremic toxins. Accordingly, toxic metabolites of uremia damage testicles and have a negative impact on spermatogenesis, semen quality, and patient fertility^[31]. These findings are inconsistent with those of other earlier studies^[13], possibly due to the difference in HD duration, which was longer in this study. This study result is supported by another study^[32], as the earlier onset and the longer

duration of uremia result in more impaired reproductive function.^[32]

In this study, the correlation between age and prolactin level was insignificant. Whereas this result is similar to a previous study^[33], it is not in concordance with the Sudanese study^[34], which said that PRL was positively correlated with age, as the mean age of the study was (40.46±9.611 years). While the Sudanese study included female patients, representing 50% of the sample size, which affected study results, the present study included younger patients whose mean age was 33.9±7.7 years, and all patients were males.

Conclusion

Erectile function and fertility are major health concerns that adversely affect the quality of life when they are affected. ED prevalence is very high among HD patients; the most common cause is an endocrinological disturbance that is mainly caused by uremia, leading to increased prolactin and a low testosterone level. Also, hormonal disturbances and uremia affect semen quality, which subsequently affects patient fertility.

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