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Assessment of sex hormones and their correlation with the quality of life in male hemodialysis patients

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Abstract. *In Chronic Kidney disease (CKD) there are various abnormalities in hormonal levels that lead to impairment of sexual functions, fertility, and pregnancy outcomes. Sex hormonal dysfunction not only affects the sexual aspect of human life but has a direct and indirect impact on other aspects like bone health, the central nervous system, and cognitive function. In this study, we looked at the testosterone and gonadotropins levels and their correlation with the quality of life using the SF-36 form.*

Methods. In this cross-sectional observational study, we included 50 male patients on hemodialysis (HD) with a dialysis vintage of at least 6 months. Serum testosterone, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) were done from the mid-week pre-hemodialysis sample. Other hematological and biochemical parameters were assessed as well. Quality of life was assessed using the SF-36 form. Further analysis was done to find the correlation between SF 36 score and hormonal levels.

Results. The mean age of our patients was 34.86±8.12 years and dialysis vintage was 24.24±18.74 months. The mean serum LH level was 8.58±3.56 mIU/ml, the mean serum FSH level was 8.9±4.05, and the mean testosterone was 217.46±96.44 ng/dl. In our study 15 patients (30%) had normal testosterone levels >270 ng/dl, 35 patients (70%) had low testosterone level (<270ng/dl). SF36 score in our study was 54.82±12.81. There was no correlation between LH, FSH levels and quality of life. However, there was a significant positive correlation between testosterone levels and SF-36 score.

Conclusion. Hypogonadism is common in HD male patients. Testosterone level has a positive correlation with SF-36 scores.

Keywords: *testosterone, quality of life, hemodialysis, sex hormones.*

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Статеві гормони та їх асоціація з якістю життя у чоловіків, які лікуються гемодіалізом

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Резюме. *Хронічна хвороба нирок (ХНН) призводить до порушення гормонального фону і, відповідно, статевих функцій, фертильності та наслідків вагітності. Статева гормональна дисфункція не тільки впливає на сексуальний аспект людського життя, але має прямий і опосередкований вплив на інші аспекти, такі як здоров'я кісток, центральної нервової системи та когнітивні функції. У цьому дослідженні ми розглянули рівні тестостерону та гонадотропіну та їх кореляцію з якістю життя за допомогою опитувальника SF-36.*

Методи. У це перехресне обсерваційне дослідження включено 50 хворих чоловічої статі з ХХН V, які лікувались методом гемодіалізу (ГД) щонайменше 6 місяців. Дослідження сироваткових концентрацій тестостерону, лютеїнізуючого гормону (ЛГ) і фолікулостимулюючого гормону (ФСГ) виконували в середині тижня перед ГД. Також оцінювали інші гематологічні та біохімічні показники. Якість життя оцінювали за формою SF-36.

Результати. Середній вік пацієнтів становив 34,86±8,12 років, тривалість діалізу 24,24±18,74 місяця. Середній рівень сироваткового ЛГ становив 8,58±3,56 мМО/мл, ФСГ – 8,9±4,05 мМО/мл, тестостерону – 217,46±96,44 нг/дл. Лише 15 (30%) пацієнтів мали референтні значення тестостерону >270 нг/дл, 35 (70%) пацієнтів мали низький рівень тестостерону (<270 нг/дл). Ми не визначили кореляції між рівнями ЛГ, ФСГ і якістю життя. Проте встановлено статистично значущий прямий кореляційний зв'язок між концентрацією тестостерону та середнім балом SF 36.

Висновок. Гіпогонадизм часто здіагностується у пацієнтів чоловічої статі, які лікуються ГД. Рівень тестостерону позитивно корелює з якістю життя пацієнтів.

Ключові слова: *тестостерон, якість життя, гемодіаліз, статеві гормони.*

Introduction. In chronic kidney disease (CKD) there are various abnormalities in hormonal levels that lead to impairment of sexual functions, fertility, and pregnancy outcomes [1]. Sex hormonal dysfunctions not only affect the sexual aspect of human life but has a direct and indirect impact on other aspects like bone health, central nervous system, cognitive function, etc. Studies have revealed that age-related endocrine dysfunction leads to cognitive decline and increases the risk of neurodegenerative diseases. As has been proven already that estrogens can be protective of cognitive function, recently androgens and gonadotropins like luteinizing hormone (LH) have been shown to modulate learning and memory [2]. Significant derangements of the hypothalamic, pituitary, and gonadal axis have been commonly identified in CKD patients [1]. To assess the different aspects of a patient's life (emotional, physical and social), a commonly used questionnaire worldwide is the Short Form 36 (SF 36) Various studies have revealed the poor quality of life in the CKD population, be it patients in early stages of CKD or patients on dialysis. Comparison of quality of life in patients receiving hemodialysis, peritoneal dialysis, or kidney transplantation has also been studied using SF 36 questionnaire [3-5]. Erectile dysfunction is seen in 20-80% of patients with CKD and about 80% of male patients on dialysis have erectile dysfunction [6]. It has been observed that quality of life improves in non-CKD patients and hypogonadism with the replacement of gonadotropin or testosterone hormones [7]. It has been observed that the quality of life is worse in patients with higher severity of erectile dysfunction [8]. In this study, we investigated testosterone and gonadotropin levels and their correlation with the quality of life using SF-36.

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The **present study aimed** to assess the sex hormonal status and its association with the quality of life in male hemodialysis patients.

Materials and Methods. After attaining ethical approval (IEC/GMC/2020/01/38) and consent of patients, in this cross-sectional observational study, 50 male patients on hemodialysis with a dialysis vintage of at least 6 months were included. All the included patients were undergoing dialysis at a single center funded by the state government and were in the age group of 18-45 years. Patients on any hormone replacement therapy, dialysis vintage less than 6 months, and age<18 or >45 years were excluded from the study.

Serum testosterone, LH, and follicle-stimulating hormone (FSH) were done from the mid-week pre-HD sample. Other hematological and biochemical parameters were assessed. Quality of life was assessed using the SF-36 form.

The data obtained was analyzed using SPSS version 24.0. Continuous variables were expressed as means (M), and the standard deviations (SD), and compared using the Student's t-test. Categorical variables were expressed as frequency and percentage and compared using the Chi-square tests (χ^2). The Spearman correlation test was used to assess the association between categorical variables. The receiver operating characteristic (ROC) analysis was performed to determine the optimal cut-off point of testosterone to predict changes in quality of life using the SF 36 form.

Results. The mean age of the patients was 34.86±8.12 years and the dialysis vintage of 24.24±18.74 months. All the patients were on thrice weekly HD with AV fistula as HD access. 12 (24%) patients were diabetic, and 1 patient was HBV positive. In our study, the mean serum LH level was 8.58±3.56mIU/ml, mean serum FSH level was 8.9±4.05, and mean testosterone was 217.46±96.44 ng/dl. In our study 15 patients (30%) had normal testosterone levels >270ng/dl, 35 patients (70%) had low testosterone level (<270ng/dl). The clinical characteristic of the patients is presented in Table 1.

Table 1

Clinical characteristics of the patients

	Mean
Age (years)	34.86 ± 8.12
Weight (kg)	52.44 ± 7.90
Vintage (months)	24.24 ±18.74
Hb (g/dl)	9.14 ± 1.68
TLC (per cmm)	7300.74 ± 2025.48
Platelet (per cmm)	208836.96 ± 61323.05
Creatinine(mg/dl)	8.80 ± 2.13
Calcium (mg/dl)	8.40 ± 1.07
Phosphorus(mg/dl)	4.51 ± 1.52
Bilirubin (mg/dl)	0.83 ± 0.26
Albumin (g/dl)	3.38 ± 0.58
IDWG (kg)	2.25 ± 0.87
Leutinizing Hormone (mIU/ml)	8.58 ± 3.56
Follicle Stimulating Hormone (mIU/ml)	8.90 ± 4.05
Testosterone (ng/dl)	217.46 ± 96.44

Abbreviations: IDWG, interdialytic weight gain; Hb, hemoglobin; TLC, total lymphocyte count.

The mean SF36 score in our study was 54.82±12.81, with 26 patients having SF 36 scores above 50, and 24 patients having scores below 50. When the anthropometric and biochemical parameters between low SF 36 and high SF 36 were compared, testosterone levels were higher in the high SF 36 group ($p<0.05$) the differences in the rest of the parameters were statistically insignificant (Table 2).

Table 2

Comparison between study parameters and SF36 score among the patients

Parameters	SF 36 < 50 (n = 24)	SF 36 > 50 (n = 26)	p-value
Age (years)	33.54 ± 8.61	36.08 ±7.60	0.274
Weight (kg)	50.46 ± 7.67	54.27 ±7.81	0.088
Height (cm)	158.75 ± 5.30	160.19 ±8.70	0.487
BMI (kg/m^2)	20.67 ± 3.18	20.53 ±2.84	0.874
Vintage (months)	28.17 ± 21.22	20.62 ±15.67	0.157
Hb (g/dl)	8.86 ± 1.88	9.40 ±1.47	0.260
TLC (per cmm)	6962.79 ± 2064.82	7612.69 ±1976.82	0.261
Platelet (per cmm)	201028.33 ± 60052.10	216044.92 ±62771.73	0.393

Continuation of Table 2

Parameters	SF 36 < 50 (n = 24)	SF 36 > 50 (n = 26)	p-value
Creatinine (mg/dl)	8.41 ± 1.80	9.15 ±2.37	0.222
Calcium (mg/dl)	8.49 ± 1.03	8.31 ±1.11	0.556
Phosphate (mg/dl)	4.58 ± 1.32	4.44 ±1.70	0.747
Bilirubin (mg/dl)	0.83 ± 0.26	0.83 ±0.27	0.986
Albumin (g/dl)	3.48 ± 0.63	3.29 ±0.53	0.248
IDWG (kg)	2.32 ± 0.92	2.19 ±0.84	0.619
LH (mIU/m)l	8.56 ± 3.78	8.56 ±2.80	1.000
FSH (mIU/ml)	9.92 ± 4.59	9.38 ±4.33	0.670
Testosterone (ng/dl)	181.00 ± 77.08	251.12 ±101.55	0.009

Abbreviations: BMI, body mass index, FSH, follicle-stimulating hormone; IDWG, interdialytic weight gain; Hb, hemoglobin; LH, luteinizing hormone; TLC, total lymphocyte count.

There was no correlation between the quality of life and LH (r = -0.04, p = 0.97), or FSH (r = 0.016, p = 0.93) levels. However, there was a significant positive correlation between testosterone levels and quality of life (r = 0.37, p = 0.009) (Fig.1).

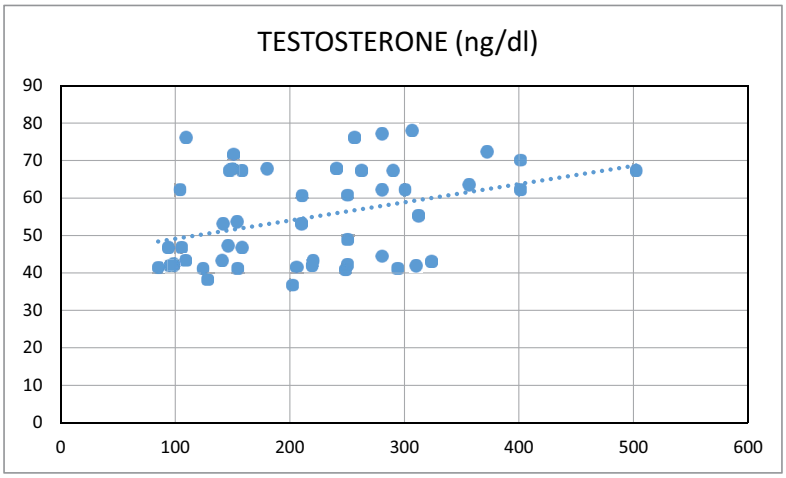

Fig. 1. The correlation between SF 36 score and testosterone levels in male HD patients.

Testosterone at a best cut off value of 146.5ng/dl could predict SF 36 >50 or SF 36 <50 with a sensitivity of 88.5 % and specificity of 45.8% (p = 0.01) (Fig. 2).

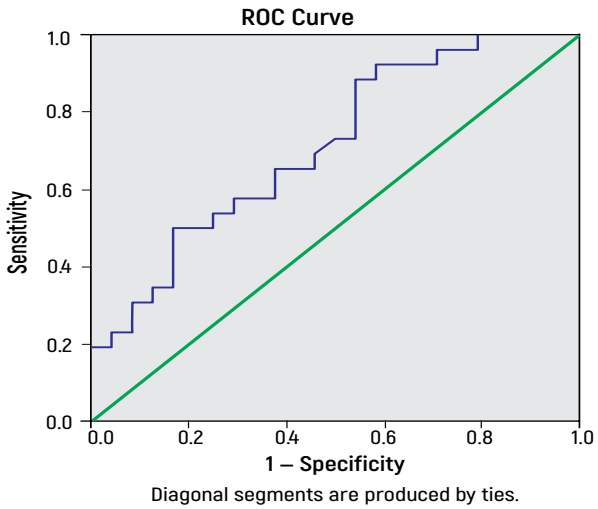

Fig. 2. Receiver-operating characteristic (ROC) curve for the cut-off value of testosterone to predict changes in quality of life using the SF 36 form.

Discussion. In the present study, we found that only 15 (30%) male HD patients had normal testosterone levels >270ng/dl, and 35 (70%) of them had low testosterone levels (< 270ng/dl). In one of the earliest studies by Guevara et al, 26 male CKD patients aged of 14-65 years were included to study gonadotropin hormonal levels (LH, FSH) [9]. The patients were subdivided based on renal replacement therapy (RRT) modality HD or peritoneal dialysis (PD), and those not on RRT. It was observed that serum LH level (21.6 ±12.2 mIU/ml) was higher in the patients on HD compared to PD or pre-dialysis patients and the control group. They found no significant difference in FSH levels among the patient groups. They also found that testosterone levels ranged between 101-426 mμg/dl (mean value 256 mμg/dl) and were lower than in the control group [9]. Contrary to the mentioned study, we found serum LH and FSH in the reference ranges. Distiller et al found that the mean basal LH levels in both HD and PD patients were significantly elevated whereas serum testosterone levels were significantly low when compared to the control group [8]. However, there was no significant difference between pre-dialysis and post-dialysis levels of hormones [8]. Eckersten et al demonstrated higher prolactin and estradiol levels in HD male patients compared to control [10]. There were no differences found for FSH and testosterone between HD patients and the control group. The level of LH in their study was in the normal range [10]. Moreover, in accordance with our findings, Carrero et al have found a testosterone deficiency in a large cohort of male HD patients [11]. Cang ven et al have demonstrated that male HD patients with normal testosterone concentration had better sexual function as assessed by the International Index of Erectile Function (IIEF) than those with testosterone deficiency [12]. Hypogonadism was seen in 11.1% of patients and patients with low testosterone levels had higher gonadotropin levels [12]. In our study, 70% of men had hypogonadism which is contrary to the aforementioned study. One of the reasons for the smaller number of hypogonadal patients could be less number of diabetics included in their study. They concluded that normalization of serum testosterone levels after administration of T-gel was an effective treatment for erectile dysfunction. In the study from Pakistan, testosterone deficiency was observed in 60% of men compared to 70% of men in our study [13].

The quality of life assessment in our study was done using the SF-36 questionnaire and we found that the mean SF-36 score in our study was 54.82 ± 12.81. No statistically significant difference was observed in LH and FSH levels between the two groups with high and low SF-36 scores. However, the testosterone levels were higher in the patients with better quality of life. We found that there was a positive correlation between SF36 scores and testosterone levels (r =0.366). Using the ROC curve, testosterone at the best cut-off value of 146.5 ng/dl could predict SF 36 >50 or SF 36 <50 with a sensitivity of 88.5 % and specificity of 45.8%. Feroze et al have observed that lower quality of life scores was associated with higher mortality risk [14]. Both the mental health and physical health dimensions of the SF-36 showed significant associations with mortality in their study. They also observed that creatinine and serum albumin levels were higher in those with a higher quality of life score quartiles [14]. Contrary to their finding, we did not find statistically significant differences in creatinine and albumin levels in patients with SF-36 scores >50 or <50. In their study, Oliveira et al observed lower quality of life scores compared to studies from the United States and Europe but higher than the scores observed in studies from Asian countries like India and Saudi Arabia [15]. Moreover, in contrast to our study, they found higher quality of life scores. Shiraishi et al included 37 male hypogonadotropic hypogonadal HD patients (mean age: 26.1years) who received gonadotrophin (n = 31) or testosterone treatment (n = 6) [7]. The SF-36 questionnaire was used to assess the quality of life at the baseline and every 6 months during the 2-year treatment period. The SF-36 scores in the patient population were lower than in the normal Japanese population. They concluded that gonadotrophin treatment for MHH was associated with significant improvements in SF-36 domains [7]. Rosas et al observed that the emotional domains of the SF-36 were more profoundly associated with erectile dysfunction than the physical domains [17]. This study highlights the fact that poor sexual function leads to poor quality of life and vice versa.

Our study has several limitations. It was an observational study with small sample size, and the hormones studied were measured at only one time point. Therefore, causality could not be established. In addition, we did not examine erectile dysfunction in the patients, which could clarify our findings on the relationship between testosterone levels and quality of life.

Conclusions. Hypogonadism is common in HD patients. Testosterone level correlates positively with SF-36 scores. Further studies with a larger cohort of patients are needed to confirm these preliminary results and validate testosterone level as a proposed biomarker of quality of life in clinical practice.

Conflict of interest. The authors declare no conflict of interest.

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Author Contributions.

Muzamil Latief: the study design, literature search, conduct and planning, data analysis, manuscript writing, and submission;

Manjusha Yadla: study design, planning, and supervision, data analysis, project writing;

Farhat Abbas: data analysis, literature search, manuscript writing.

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