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# LUTEINIZING HORMONE AND FOLLICULAR STIMULATING HORMONE LEVELS AFTER SUCCESSFUL KIDNEY TRANSPLANTATION IN SUDANESE MALE

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## ABSTRACT

Male patients with chronic kidney disease often exhibit the biological and clinical hallmarks of an abnormal hypothalamus–pituitary–gonadal axis. It is known that dialysis does not reverse this impaired endocrine status, however the impact of kidney transplantation (KT) is still controversial. The aim of this study was to investigate the levels of serum gonadotropins (LH and FSH) after immunosuppressive drugs of KT. **Methods**: Descriptive analytical case control study was led in AL Khartoum state. Blood hormones levels were assayed by immunoassays in 45 men (mean age: 33 years) and at 6 months post-KT. These data were compared with those from 45 healthy men (mean age: 33 years) as controls. The main outcome measure was the between-groups differences in hormones levels. A second criterion was the comparison of patients and controls hormones levels according to the immunosuppressive drugs. **Results**: Serum FSH and LH level restored to the normal ranges in all kidney transplant recipients, When the correlation between the level of the reproductive hormones in kidney transplanted patients, the findings showed that a significant negative correlation (r=-0.047, P>0.05) was found between level of LH and age of patients While a significant positive correlation (r=0.171, P>0.05) was found between level of FSH and time after transplantation, positive correlation (r=0.041, P>0.05) was found between level of LH and time after transplantation in men patients and positive correlation (r=0.21, P>0.05) was found between level of FSH and age of patients. The comparisons between levels of the LH, FSH

and immunosuppressive drugs after transplantation in men patients and controls indicated increase LH in patients who they took tacrollimus drug and the levels of the FSH not significant in patients who they took cyclosporine and tacrollimus drugs. **Conclusions**: Successful kidney transplantation could effectively improve pituitary gonadal hormone disturbance and sexual and reproductive dysfunctions of ESRD patients.

**KEYWORDS:** Kidney transplantation, Gonadotropins, LH, FSH, Cyclosporine, Tacrollimus, and Immunosuppressive Drugs.

- **INTRODUCTION**

Among the treatments available for end stage renal disease (ESRD), hemodialysis, peritoneal dialysis, and kidney transplantation (KT), the latter is a successful treatment modality for ESRD and the preferred mode of renal replacement therapy. Male patients with ESRD commonly experience sexual dysfunction and infertility as a result of endocrine aberrations, vasomotor dysfunction, prescribed medications, and psychological factors.[1.2] Alterations on sex steroid production and metabolism are already seen when moderate reductions in the glomerular filtration rate (GFR) arise.[3] It has been reported that the period of ESRD preceding KT is associated with disorders in hypothalamic-pituitary gonadal (HPG) function in both genders.

In male patients, there is high prolactin (PRL) level (hyperprolactinaemia)[4], abnormal gonadotropin-releasing hormone (GnRH) pulsatility[1], high luteinizing hormone (LH) and follicle-stimulating hormone (FSH) values, low testosterone levels and reduced spermatogenesis.[5] Although abnormalities in the HPG axis are well recognized in both genders during ESRD (3.1), Several studies have shown that male HPG dysfunction was found to be either reversed[6], differently improved[7] or altered after successful KT[8], However there are few studies concerning serum luteinizing hormone and follicle stimulating hormone after kidney transplantation in Sudanese populations. The present paper investigated post-operative serum LH and FSH hormones in a Sudanese population to see whether or not successful kidney transplantation.

## 2. MATERIALS AND METHODS

### 2.1. Materials

#### 2.1.1. Study design

This is a descriptive analytical case control study.

### 2.1.2. Study area

This study was conducted in Khartoum state.

### 2.1.3. Study populations

The study included 45 renal transplantation recipients as test group and 45 healthy individuals as control (mean age of 30 ± 10 years for both groups).

#### 2.1.3.1. Inclusion criteria

Male with renal transplantation taking cyclosporine or tacrollimus drugs will be included in this study.

#### 2.1.3.2. Exclusion criteria

Males with diabetes, hypertension, other diseases that might significantly impair sexual or reproductive functions, males who take hormonal treatment and no other possible secondary causes for male infertility were excluded.

### 2.1.4. Ethical consideration

Individuals involved in this study were informed by the study and its importance. This study was approved by the Research Committee of Medical Laboratory Science College Al-Neelain University.

### 2.1.5. Statistical analysis

Data were summarized, presented and analyzed using statistical package for the social science (SPSS) software program version 16. Data are expressed as mean ± SD. Student's t-test was used to compare the group of patients and controls. Linear correlation coefficients and their significance were determined to assess the dependence between endocrine features and age, duration of transplant. The level of significance was determined ATP<0.05(14).

### 2.1.6. Sampling

5 milliliters of venous blood was collected from each male enrolled in the study in plain tube, serum was separated immediately after coagulation then stored frozen at - 20 c. The deep frozen serum samples were thawed, kept to reach room temperature, and brought for the estimation of hormones.

### 2.2. Methods

Estimation of testosterone, LH, and FSH was done by Enzyme Linked Immune Sorbent assay using an Instrument MAPLAP plus (ITALY).

#### 2.2.1. Estimation of Follicle Stimulating Hormone

The FSH Quantitative test Kit is based on the principle of a solid phase enzyme linked immunosorbent assay. The assay system utilizes a polyclonal anti -FSH antibody for solid phase (micro titer wells) immobilization and a mouse monoclonal anti FSH antibody in the antibody-enzyme (horseradish peroxidase) conjugate solution. The test sample was allowed to react simultaneously with the antibodies, resulting in FSH molecules being sandwiched between the solid phase and enzyme-linked antibodies. After 60 minutes incubation at room temperature, the wells are washed to remove unbound labeled antibodies. A solution of TMB was added and incubated for 20 minutes, resulting in the development of a blue color. The color development was stopped with the addition of 2N HCL, and the color was changed to yellow and measured spectrophotometric ally at 450nm. The concentration of FSH was directlyproportional to the color intensity of the test sample.

#### 2.2.2. Estimation of Luteinizing Hormone

The LH Quantitative test Kit is based on the solid phase enzyme linked immunosorbent assay. The assay system utilizes one anti- LH antibody for solid phase (micro titer wells) immobilization and another mouse monoclonal anti-LH antibody in the antibody enzyme (horseradish peroxidase) conjugate solution. The test sample was allowed to react simultaneously with the antibodies, resulting in LH molecules being sandwiched between the solid phase and enzyme-linked antibodies. After 60 minutes incubation at room temperature, the wells are washed to remove unbound labeled antibodies. A solution of TMB was added and incubated for 20 minutes, resulting in the development of a blue color. The color development was stopped with the addition of 2N HCL, and the color was changed to yellow and measured spectrophotometric ally at 450nm. The concentration of LH was directly proportional to the color intensity of the test sample**.**

## 3. RESULTS

The statistical analysis was done by SPSS and the results were as follow:

### 3.1. Effect of cyclosporine and tacrollimus drugs on LH level

Comparison of means showed a significantly increase LH level in case was toke tacrollimus versus control groups (Figure 1).

### 3.2. Effect of cyclosporine and tacrollimus drugs on FSH level

Comparison of means showed not significantly in FSH level in case versus control groups (Figure 2).

### 3.4. Person's Correlation Results

3.4.1. Follicular stimulating hormone correlated positively with age of patients as presented in (Figure 3).

3.4.2. Luteinizing hormone correlated negatively with age of patients as presented in (Figure 4).

3.4.3. Follicular stimulating hormone correlated positively with time after transplantation (duration) as presented in (Figure 5).

3.4.4. Luteinizing hormone correlated positively as presented in (Figure 6).

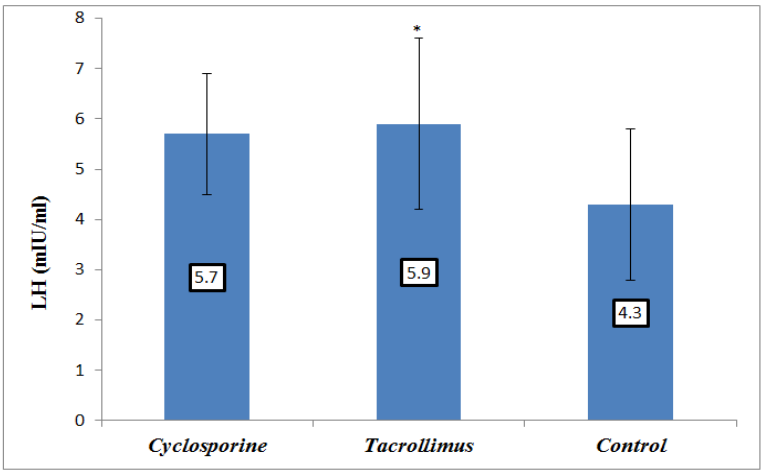


**Figure 1: LH level in case versus control groups.**

Significant indicated increase LH in patients who they took tacrollimus drug.

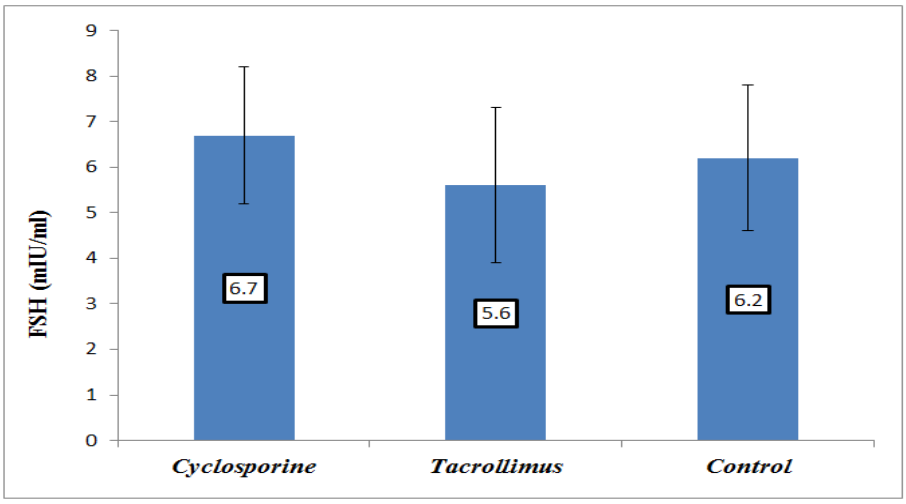


**Figure 2: FSH level in case versus control groups.**

Indicated not significant with cyclosporine and tacrollimus drugs.

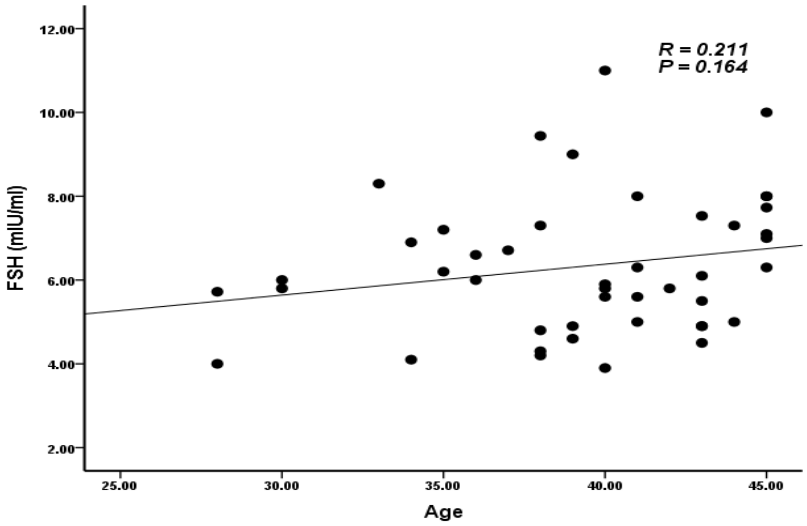


**Figure 3: Correlation between Follicular stimulating hormone level and Age**

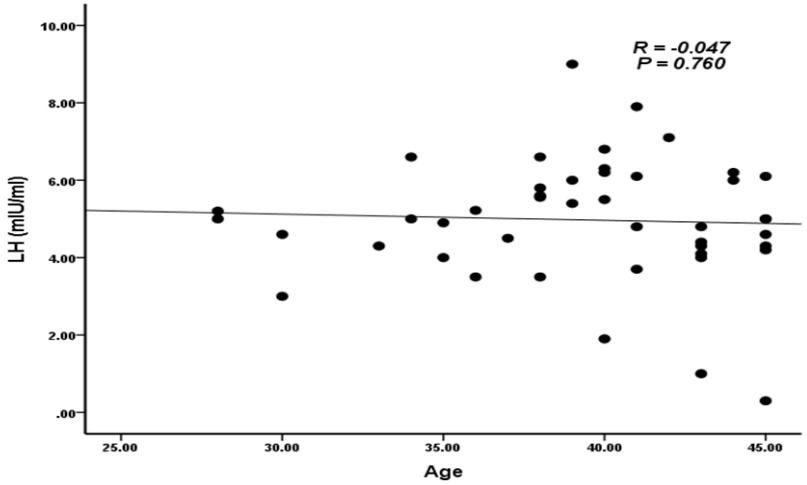

**Figure 4: Correlation between luteinizing hormone level and Age**

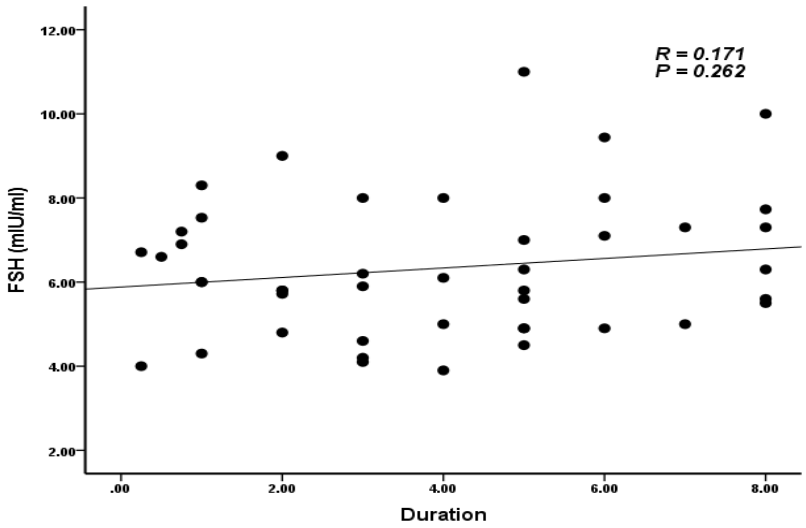


**Figure 5: Correlation between Follicular stimulating hormone level and Duration**

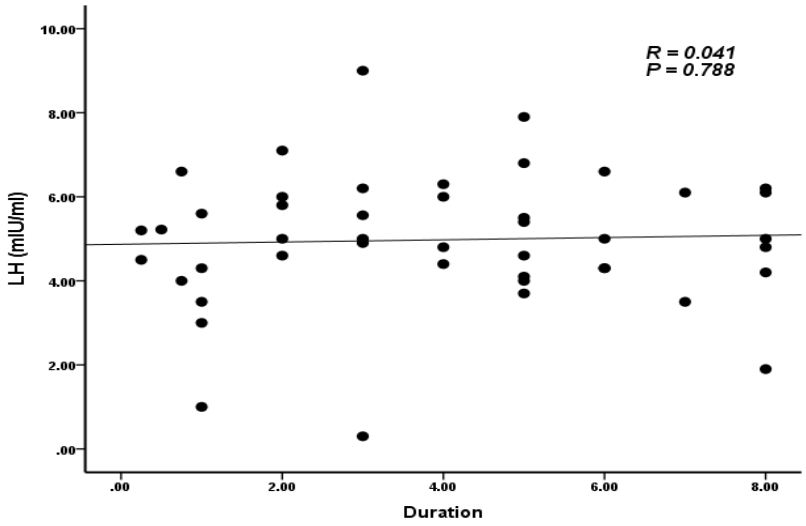


**Figure 6: Correlation between luteinizing hormone level and Duration**

## 5. DISCUSSION

Kidney transplantation was reported to restore endocrine function, but study results are discordant. The restoration of hormonal profiles after successful KT is still controversial. The results of a previous study have suggested that KT restores the balance in the HPG axis.[7] It has been reported that the HPG axis after KT is mostly influenced by the quality of allograft function, the use of immunosuppressive treatments and general health conditions.[9,10] In 2007, Anantharaman *et al*. found that successful KT may restore normal sexual function, especially in younger patients.[11] In 2008, Barroso *et al.* stated that kidney transplants improve sexual function of patients compared with ESRD on hemodialysis.[12] These data

differed from those of other authors who found persistent abnormalities of the HPG axis function in KT recipients with well-functioning allografts.[13.14]

In the present study which investigated level of reproductive hormones in men after successful KT found normal LH and FSH levels in transplanted men as compared to controls, results showed that there were no significant differences in levels of these hormones between male patients and controls. These results are in line with those of Samojlik *et al.*[6] who found that, three months after transplantation plasma LH, and FSH levels were restored toward normal. A trend toward normal levels of these hormones in men after KT suggests improvement of testicular function. Immunosuppressive drugs may influence the restoration of hormonal profiles after successful KT. Tondolo *et al.*[15] were able to evaluate the hormonal status of successful renal transplant recipients who were treated with different immunosuppressive agents. They concluded that immunosuppressive therapies may influence the restoration of normal levels of gonadal hormones after KT. In several studies, erythropoietin therapy has been reported to cause normalization of the pituitary gonadal feedback mechanism with reduced plasma concentrations of LH and FSH.[16,17]

In the present study a relationship between levels of the reproductive hormones in men kidney transplanted patients and immunosuppressive drugs was studied, the results showed that a significant and a low significant positive correlation were found between levels of FSH and age (r=0.21), level of FSH and time after transplantation (duration) (r=0.171 ) in men patients, While negative correlation was found between levels of LH and age (r=-0.047) and positive correlation (r=0.041) with time after transplantation (duration) in men patients. This positive significant correlation indicates that increased serum FSH levels in the studied cases suggest conditions that affect by the age in increased levels of this hormone in the blood of men patients. On the other hand, the significant negative correlation indicates that decreased LH level in these patients (men).

The comparisons between levels of the LH, FSH and immunosuppressive drugs after transplantation in men patients and controls indicated increase LH in patients who they took tacrollimus drug and the levels of the FSH not significant in patients who they took cyclosporine or tacrollimus drugs.

## 6. CONCLUSIONS

A normalization of the levels of the reproductive hormones (LH, FSH,) in KT recipients is probably multifactorial, being influenced by immunosuppressive treatments, age and duration of transplantation. This restoration of normal levels of these hormones suggests improvement of testicular function in men. The slightly elevated FSH level in men after KT was explained mostly by a decreased metabolic clearance and increased production.

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