MJPS….Vol.(2)….No(1)….December 2014

Sexual hormone abnormalities in patients with chronic renal failure

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Abstract

Present study was conducted at Dialysis unit in Al-Sadder medical city /Al-najaf Al-Ashraf during the period from July till November, 2012,wich aims to determined the effect of chronic renal failure on gonadal hormone in male by using 70 male subjects divided into two groups 50 of them had chronic renal failure and the remaining 20 subjects were normal healthy individuals served as a control .

The result of this study revealed that significant increased $p<0.05$ in serum FSH 30.651 ± 0.12 (U/L), renal failure patients compared with healthy group 9.363± 0.65 (U/L). and significant increased $p<0.05$ of serum LH concentration in renal failure patients 17.452± 0.22(U/L) as compare with HT group 6.185±0.43(U/L). also the study showed significant increase $p<0.05$ of serum PRL concentration in renal failure patients 29.779 ± 0.58(Ug/L) as compare with HT group 8.188± 0.33

(Ug/L) .

1.Introduction

Gonadal function is significantly affected in many acute and chronic systemic diseases such as kidney disease. As the function of the testes and the ovaries is determined by the integrity of the hypothalamic–pituitary–gonadal axis, it is obvious that a systemic disease may affect one or more levels of the axis in such a manner that the gonadal dysfunction may have various clinical and laboratory manifestations (Asterios and Faidon, 2005).

Kidney disease can cause physical and emotional changes that may affect your sex life. The chemical changes that occur in your body with kidney disease affect hormones, circulation, nerve function and energy level. These changes usually lower sexual interest and/or sexual ability (National Kidney Foundation,2013). Endocrine abnormalities are a common feature of chronic renal insufficiency, changes of androgen synthesis and metabolism develop early after the onset of renal insufficiency and are likely to be caused by primary hypogonadism anduor disturbances of the hypothalamic–pituitary axis(Hedef and Maysaa, 2009).

Uremia affects local amino acid neurotransmitter outflow in hypothalamus, significantly affecting the release of GnRH and hence affecting gonadotrophin synthesis and secretion in males, the plasma LH level is elevated in hemodialysis patients compared to healthy controls. This increased level is due to prolonged half-life of immunoreactive and bioactive LH as well as increased secretion of immunoreactive LH, Similar to LH, FSH levels

are normal to elevated in CKD, Serum prolactin level rise correlates with decline in glomerular filtration rate. Increase in serum prolactin levels is primarily due to decreased dopaminergic inhibition of prolactin release from pituitary gland and secondarily due to decreased LHRH release (Manish and Raja., 2012).

3.Subjects and Methods

The study was conducted on 70 male subjects divided into two groups 50 of them had chronic renal failure and the remaining 20 subjects were normal healthy individuals served as a control. The patients were collected from the Dialysis unit in Al-Sadder medical city /Al-najaf Al-Ashraf during the period from July till November, 2012. Blood samples were drawn by trained nurses or other health care professionals and freezing at -20C to keep serum stable for a few months, Enzyme linked immuno assay (ELISA) was used for the measurement of serum LH, FSH and PRL.

3.1Automated Laboratory Methods

3.1.1 Serum LH estimation

This assay executed with specific kit for test ,supplied by (Immuno - Biological Laboratories, IBL-America. RE52101).

1. MATERIALS PROVIDED

Reagent	Quantity	Reagent	Quantity
Microtiter wells	1	Stop Solution	1 x 12 ml
Standard	6 x 0.7 ml	Instruction manual	1
TMB Substrate	1 x 12 ml	Adhesive Strip	2
Enzyme-Conjugate	1 x 12 ml	Wash Buffer	1 x 25 ml

2. Assay procedure

1. Secure the desired number of coated Microtiter Wells in the holder.
2. Dispense 25 µl LH Standards (0; 10; 20; 40; 100; 200 mIU/ml), controls and serum specimen with new disposable tips into appropriate wells.
3. Dispense 100 µl Anti-LH Enzyme-Conjugate into each well.
4. Thoroughly mix for 10 seconds. It is important to have a complete mixing in this step.
5. Incubate for 30 minutes at room temperature.
6. Briskly shake out the contents of the wells.
7. Rinse the wells 5 times with dist. water.
8. Strike the wells sharply on absorbent paper to remove residual water droplets.
9. Add 100 µl of Substrate Solution to each well, at timed intervals.
10. Incubate for 10 minutes at room temperature.

11. Stop the enzymatic reaction by adding 50 µl of Stop Solution to each well,at the same timed intervals as in step 9.

12. Read the OD at 450±10 nm with a microtiterplate reader.

3.CALCULATION OF RESULTS

1.Calculate the average absorbance values for each set of reference standards, controls and patient samples.

2.Construct a standard curve by plotting the mean absorbance obtained from each reference standard against its concentration in mIU/ml with absorbance value on the vertical(Y) axis and concentration on the horizontal (X) axis.

3.Using the mean absorbance value for each sample determine the corresponding concentration of LH in mIU/ml from the standard curve. Depending on experience and/or the availability of computer capability, other methods of data reduction may be employed.

3.1.2 Serum FSH estimation

This assay executed with specific kit for test, supplied by (Immuno - Biological Laboratories, IBL-America. RE52121).

1. MATERIALS PROVIDED

Reagent	Quantity	Reagent	Quantity
Microtiter wells	1	Stop Solution	1 x 12 ml
Standard	6 x 0.7 ml	Instruction manual	1
TMB Substrate	1 x 12 ml	Adhesive Strip	2
Enzyme-Conjugate	1 x 12 ml	Wash Buffer	1 x 25 ml

2. Assay procedure

1.Secure the desired number of coated Microtiter wells in the holder.

2. Dispense 25 µl FSH Standards (0; 5; 10; 20; 50; 100 mIU/ml), controls and serum specimen with new disposable tips into appropriate wells.

3.Dispense 100 µl Anti-FSH Enzyme-Conjugate into each well.

4.Thoroughly mix for 10 seconds. It is important to have a complete mixing in this step.

5. Incubate for 30 minutes at room temperature.

6. Briskly shake out the contents of the wells.

7. Rinse the wells 5 times with Aqua dest.

8.Strike the wells sharply on absorbent paper to remove residual water droplets.

9. Add 100 µl of Substrate Solution to each well, at timed intervals.

10. Incubate for 10 minutes at room temperature.

11. Stop the enzymatic reaction by adding 50 µl of Stop Solution to each well, at the same timed intervals as in step 9.
12. Read the OD at 450±10 nm with a microtiterplate reader.

3.CALCULATION OF RESULTS

1.Calculate the average absorbance values for each set of reference standards, controls and patient samples.
2.Construct a standard curve by plotting the mean absorbance obtained from each reference standard against its concentration in mIU/ml with absorbance value on the vertical(Y) axis and concentration on the horizontal (X) axis.
3.Using the mean absorbance value for each sample determine the corresponding concentration of FSH in mIU/ml from the standard curve. Depending on experience and/or the availability of computer capability,other methods of data reduction may be employed.

3.1.3 Serum PRL estimation

This assay executed with specific kit for test ,supplied by (Immuno - Biological Laboratories, IBL-America. RE52131).

1. MATERIALS PROVIDED

Reagent	Quantity	Reagent	Quantity
Microtiter wells	1	Stop Solution	1 x 12 ml
Standard	6 x 0.7 ml	Instruction manual	1
TMB Substrate	1 x 12 ml	Adhesive Strip	2
Enzyme-Conjugate	1 x 12 ml	Wash Buffer	1 x 25 ml

2. Assay procedure

1. Secure the desired number of coated Microtiter Wells in the holder.

2. Dispense 25µl Prolactin Standards (0; 5; 20; 50; 100; 200ng/ml), controls and serum specimen with new disposable tips into appropriate wells.

3. Dispense 100µl anti- Prolactin Enzyme-Conjugate into each well.

4. Thoroughly mix for 10 seconds. It is important to have a complete mixing in this step.

5. Incubate for 30 minutes at room temperature

6. Briskly shake out the contents of the wells.
7. Rinse the wells with 300µl of Aqua dest. 5 times.
8. Strike the wells sharply on absorbent paper to remove residual water droplets.
9. Add 100µl of Substrate Solution to each well, at timed intervals.
10. Incubate for 10 minutes at room temperature.
11. Stop the enzymatic reaction by adding 50µl of Stop Solution to each well, at the same timed intervals as in step 9.
12. Read the OD at 450 +- 10nm with a microtiterplate reader.

3.CALCULATION OF RESULTS

1. Construct a standard curve by plotting the mean absorbance obtained from each reference standard against its concentration in ng/ml with absorbance value on the vertical (Y) axis and concentration on the horizontal (X) axis.
2. Calculate the average absorbance values for each set of reference standards, controls and patient samples.
3. Using the mean absorbance value for each sample determine the corresponding concentration of Prolactin in ng/ml from the standard curve. Depending on experience and/or the availability of computer capability, other methods of data reduction may be employed.

3. The Result

3.1 Relation between FSH of renal failure patients and healthy group.

Figure (3-1) shows comparison between renal failure patients and healthy group. This result revealed the significant increased $p<0.05$ in serum FSH 30.651±0.12 (U/L), renal failure patients compared with healthy group 9.363± 0.65 (U/L).

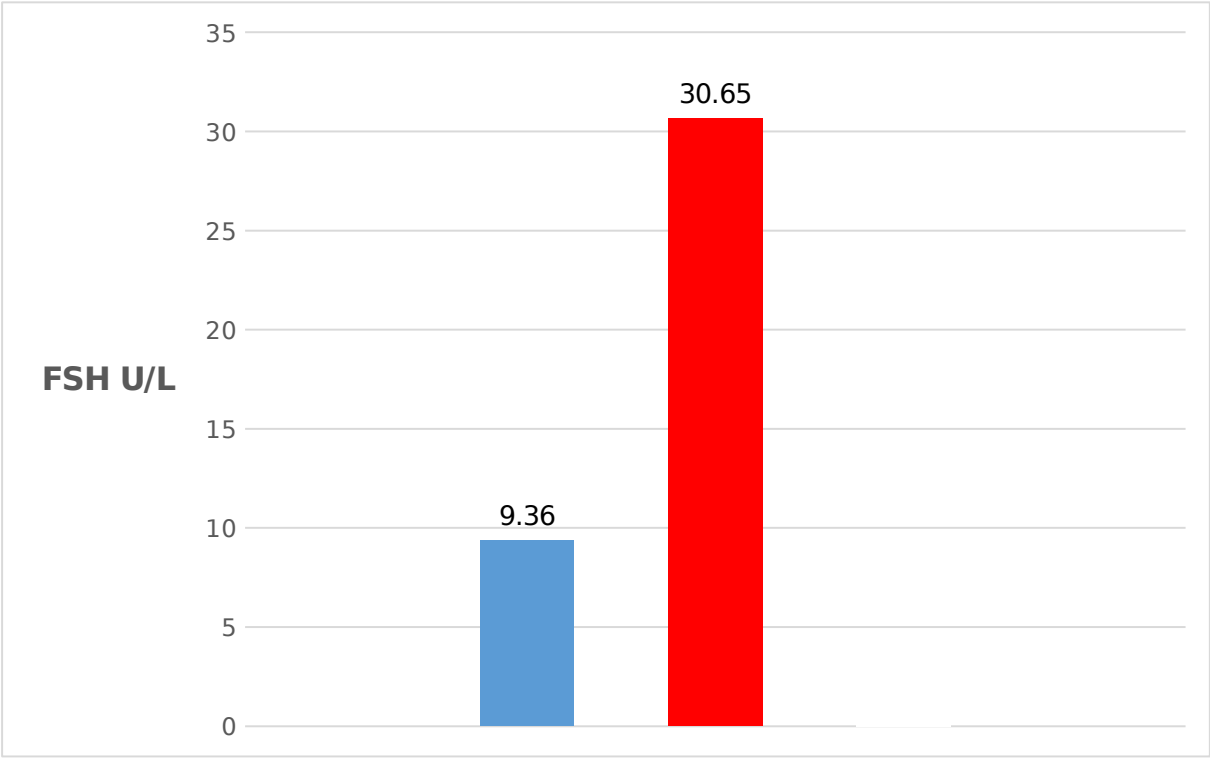

Figure (3-1) comparison between FSH level of kidney failure and Healthy group.

3.2 Relation between LH of renal failure patients and healthy group.

The result in figure (3-2) shows comparison between renal failure patients and healthy group where as significant increased $p<0.05$ of serum LH concentration in renal failure patients 17.452± 0.22(U/L) as compare with HT group 6.185 ± 0.43(U/L).

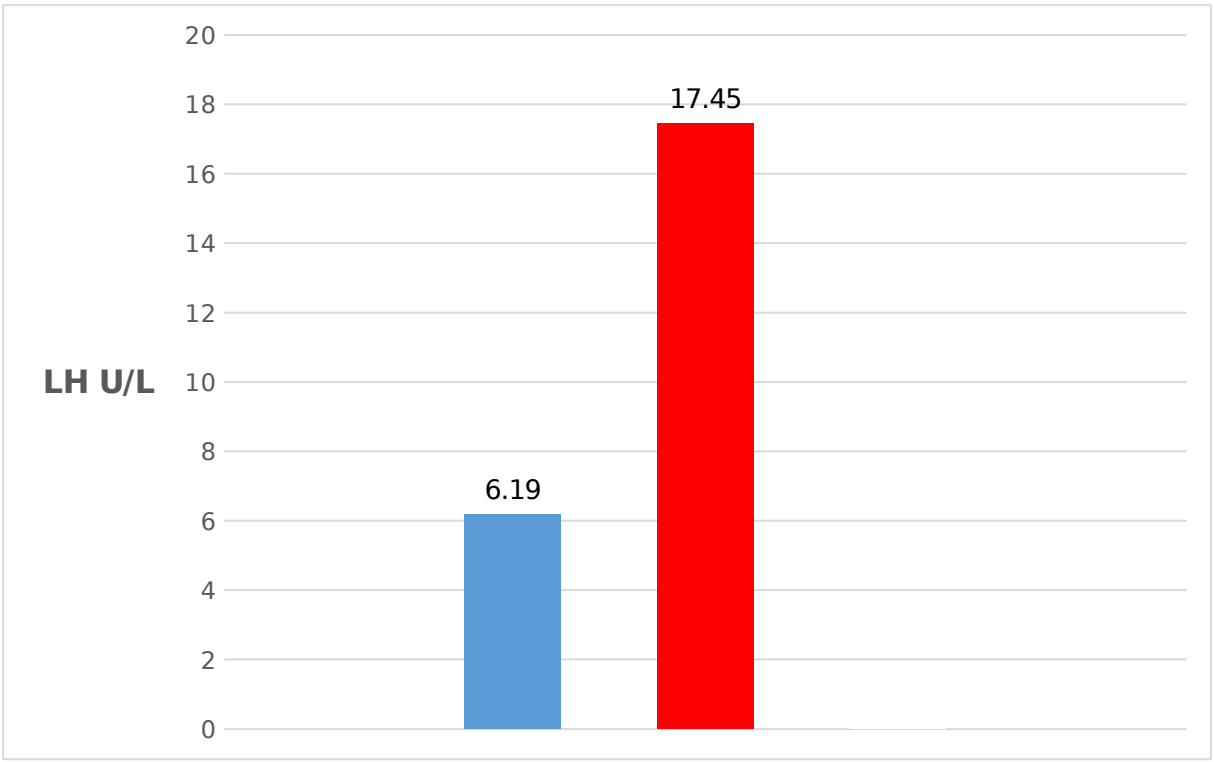

Figure (3-2) comparison between LH level of kidney failure and Healthy group.

3.3 Relation between PRL of renal failure patients and healthy group.

The Result of figure (3-3) shows comparison between renal failure patients and healthy group where as significant increase $p<0.05$ of serum PRL concentration in renal failure patients 29.779 ± 0.58(Ug/L) as compare with HT group 8.188± 0.33 Ug/L) .

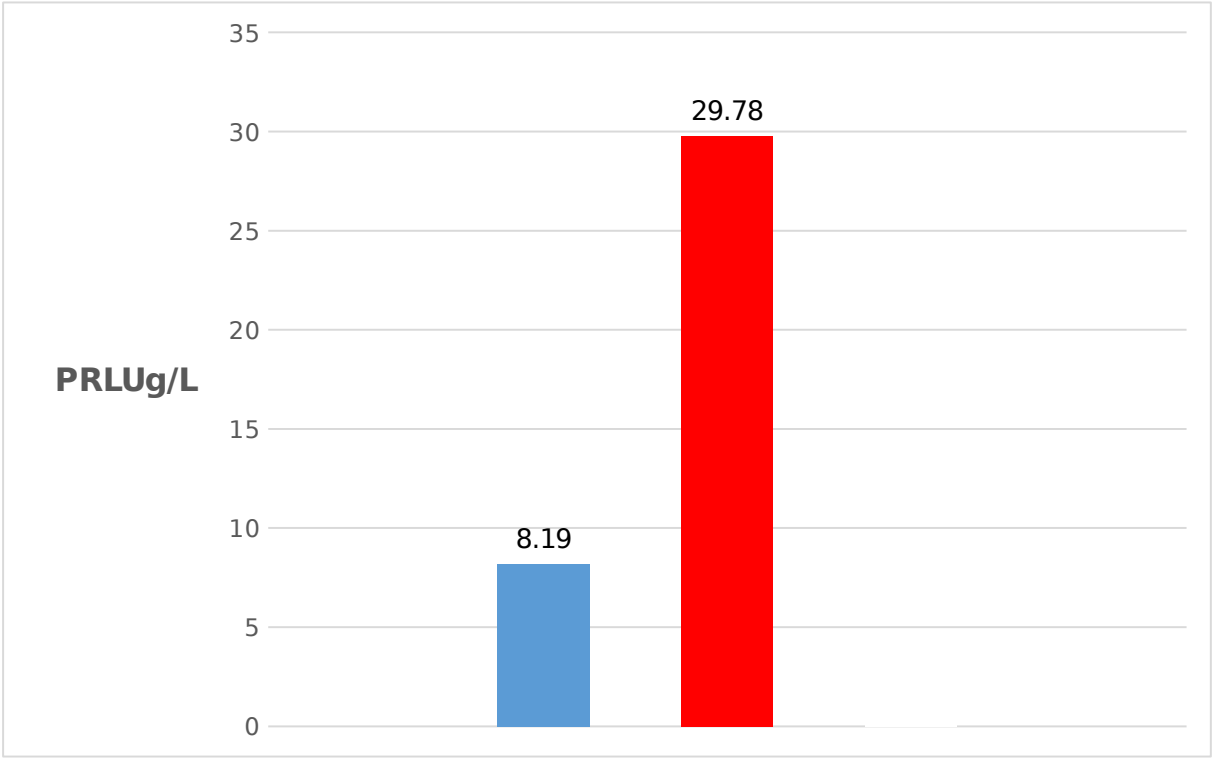

Figure (3-3) comparison between PRL level of kidney failure and Healthy group.

5. The Discussion

The result of present study shown elevated level of LH, FSH and PRL hormones ,this study in accordance with Alice *etal.,*(2002); Hamoud *etal.,*(2012)who said that elevated serum level of LH ,FSH and PRL because of decreased metabolic clearance of this hormones and a circulating LH-receptor inhibitor was suggested, which might contribute to Leydig-cell resistance and impaired feedback mechanism at the hypothalamic–pituitary level, Both LH and FSH are under control of gonadotropin releasing hormone (GnRH), but the control of FSH secretion is more complex since inhibin B, a hormone produced from testicles which level is proportional to spermatogenesis, has a negative feedback effect on pituitary FSH secretion. Elevated FSH level, pointed towards the possibility that these patients had impaired spermatogenesis.

Also BIFF (1999); Guang *etal.,* (2010) reported that the excess LH secretion in this setting is thought to result from the diminished release of testosterone from the Leydig cells, since testosterone normally leads to feedback inhibition of LH release. Elevated FSH levels are probably the result of decreased testosterone and inhibin, a Sertoli cell product. The plasma FSH concentration tends to be highest in those uremic patients with the most severe damage to seminiferous tubules and presumably the lowest levels of inhibin (Mahboob etal., 2011), The basal levels of serum prolactin are elevated in the majority of uremic patients, and the response to thyrotropin-releasing hormone (TRH) is reduced and delayed The mechanisms for the hyperprolactinemia in chronic renal failure, Increased autonomous production rate of prolactin is a major mechanism for the hyperprolactinemia but decreased metabolic clearance rate may also play a role also the state of secondary hyperparathyroidism of CRF may contribute to the increased production rate of prolactin, because PTH stimulates prolactin secretion the treatment of CRF patients with erythropoietin was associated with a decreased in serum prolactin levels.

In other hand the angiotensin II (Ang II) system is also involved in the control of anterior pituitary hormone secretion, through affecting the secretion of releasing and inhibitory factors into the hypophyseal portal vessels. Ang II controls the release of LH and PRL (Marianne., 1992).

From all reasons Hedef and Maysaa, (2009); Nihal etal., (2008)who said that Patients with renal insufficiency show, from the onset of their disease, a pattern of hormonal changes resulting from complex disturbances at the hypothalamic, pituitary and gonadal level . The causes appear to be multifactorial, with clear contribution of comorbidities and therapy. This endocrine dysfunction can only partially be influenced by renal replacement therapy, such as hemodiaylsis or kidney transplantation.

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الشذوذ في الهرمونات الجنسية لدى المصابين بمرض الفشل الكلوي المزمن

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الخلاصة :

اجريت الدراسة الحالية في وحدة الغسل الكلوي التابعة لمدينة الصدر الطبية /النجف الاشرف للمدة من شهر تموز ولغاية شهر كانون الاول للعام 2012م . هدفت الدراسة لمعرفة تأثير مرض الفشل الكلوي المزمن على الهرمونات الجنسية لدى الذكور, باستخدام (70) حالة من الذكور قسموا الى مجموعتين الاولى تتألف من (50) حالة يعانون من مرض الفشل الكلوي المزمن والثانية تتألف من (20) حالة لأشخاص ذوي صحة جيدة استخدمت كمجموعة سيطرة .اظهرت نتائج الدراسة زيادة معنوية ($p<0.05$) لمستوى هرمون FSH المصلي فكانت (30.651 ± 0.12)U/L لأشخاص مصابون بالفشل الكلوي المزمن بالمقارنة مع مجموعة السيطرة والتي بلغت 9.363± 0.65 (U/L) كما بينت نتائج الدراسة وجود زيادة معنوية ($p<0.05$) لمستوى هرمون LH للمجموعة

المصابون بالفشـل الكلـوي المزمـن حيـث بلغـت 17.452± 0.22(U/L) بالمقارنة مع مجموعة السـيطرة الاصـحاء اذ بلغـت 6.185 ± 0.43(U/L)

كما بينت النتائج وجـود ارتفـاع معنـوي ($p<0.05$) لمسـتوى هرمـون PRL للمجموعة المصابون بمرض الفشل الكلوي المزمن اذ بلغـت 29.779 ± 0.58(Ug/L) بالمقارنة مع مجموعة السيطرة التي بلغت 8.188± 0.33 (Ug/L) .)