

# Pituitary-gonadal dysfunction in uremic men on maintenance hemodialysis

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## ABSTRACT

**Objective:** To examine serum prolactin (PRL), luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels in male patients with chronic renal failure (CRF) undergoing maintenance hemodialysis (HD) and their roles in the pathogenesis of infertility encountered in patients with CRF.

**Design:** Cross-sectional study.

**Setting:** Artificial Kidney and Dialysis Unit at Ibn-Sena teaching hospital, Mosul, during the period from July to September 2002.

**Subjects:** Thirty male patients with CRF undergoing maintenance HD and 30 apparently healthy volunteers (control group) were included in this study.

**Method:** Complete history and physical examination was performed for every patient included in this study with special emphasis on duration of illness, marital status and fertility. Serum PRL, LH, FSH levels were measured; unpaired t-test was used to assess the difference in the mean of serum level of these hormones between patients with CRF and control group.

**Results:** Serum PRL, LH and FSH levels were significantly higher ( $P < 0.0001$ ,  $P < 0.0001$  and  $P < 0.0001$ ) in patients with CRF in comparison with the control group.

**Conclusion:** Abnormally high levels of serum PRL, LH and FSH are common in patients with CRF undergoing maintenance HD. This abnormality may play a role in the pathogenesis of infertility in these patients.

## الخلاصة

**الأهداف:** تعيين المستوى المصلي للهرمون اللبني ، الهرمون المصفر والهرمون المحفز للجريب لدى المرضى الذكور المصابين بعجز الكلية المزمن والذين يعالجون بطريقة التنقية الدموية المستمرة ودور تلك الهرمونات في حالات العقم لدى هؤلاء المرضى .

**التصميم:** دراسة مقطعية .

**المكان:** وحدة الكلية الاصطناعية لمستشفى ابن سينا التعليمي في الموصل .

**الزمان:** من بداية شهر تموز إلى نهاية شهر أيلول ٢٠٠٢ .

**العينات:** ثلاثون مريضاً من الذكور المصابين بعجز الكلية المزمن والمعالجين بطريقة التنقية الدموية المستمرة وعينة ضابطة مكونة من ٣٠ شخصاً من الأصحاء .

**الطريقة:** تم جمع المعلومات وإجراء الفحص السريري لجميع المشاركين في الدراسة كما تم قياس المستوى المصلي للهرمون اللبني والهرمون المصفر والهرمون المحفز للجريب وتم استخدام اختبار - t - لمقارنة النتائج .

**النتائج:** أظهرت الدراسة وجود زيادة إحصائية بقيمة معنوية في مستوى الهرمون اللبني ( $P < 0.0001$ ) ، الهرمون المصفر ( $P < 0.0001$ ) والهرمون المحفز للجريب ( $P < 0.0001$ ) لدى المرضى المصابين بعجز الكلية المزمن بالمقارنة مع العينة الضابطة .

**الاستنتاج:** نستطيع القول بأن ارتفاع المستوى المصلي للهرمون اللبني والهرمون المصفر والهرمون المحفز للجريب حالة مألوفة لدى المرضى الذكور المصابين بعجز الكلية المزمن والمعالجين بطريقة التنقية الدموية المستمرة وأن هذه الزيادة قد يكون لها دور ما في حالة العقم التي يعاني منها هؤلاء المرضى .

**A**dequate dialytic therapy together with proper medical care strategies have resulted in improvement of both the duration and

quality of life in patients with end stage renal disease<sup>(1)</sup>. However, patients with end stage renal disease continue to manifest a variety of systemic complications which are

specifically related to uremia, dialysis or both of them. There is accumulating evidence about involvement of the pituitary-gonadal axis in patients with end stage renal disease. Recent studies have shown that men on dialysis have severe spermatogenic damage and partial or complete impotence<sup>(2)</sup>. Since the kidney plays an important role in the catabolism and excretion of hormones, it is not surprising that people with CRF have an abnormal hormone level<sup>(3)</sup>.

The purpose of this study is to assess the serum level of PRL, FSH and LH in male patients with CRF undergoing maintenance HD and to evaluate the role of these hormones in the pathogenesis of infertility in these patients.

## PATIENTS AND METHODS

Thirty male patients with CRF who were attending the Artificial Kidney and Dialysis Unit at Ibn-Sena teaching hospital for maintenance HD during the period from July 2002 to September 2002 were included in this study. Their ages range from 18-67 years (mean  $\pm$ SD, 36.96  $\pm$  12.2). A control group of 30 apparently healthy subjects aged 19-64 years (38.3  $\pm$  11.6) were similarly assessed for comparison. Complete history and physical examination was done for all participants in

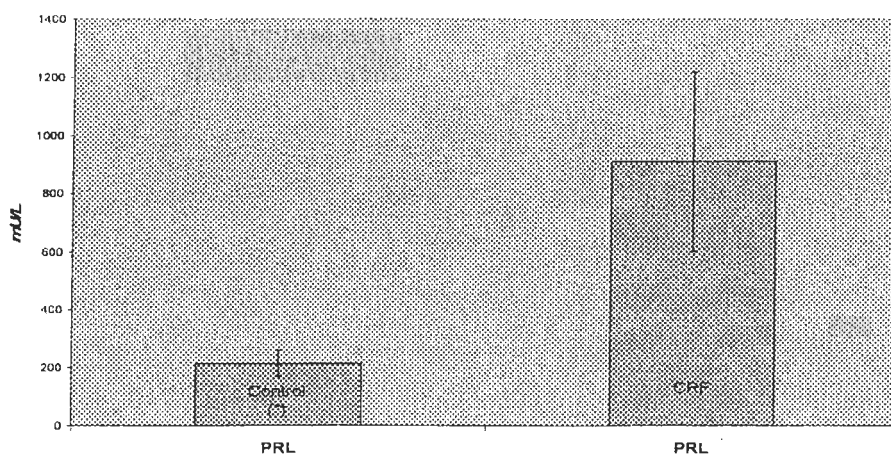
the study with special emphasis on duration of illness, marital status and fertility. Five ml of venous blood was drawn into plain tube from each subject included in the study by venipuncture. After separation of the serum by centrifugation the serum sample was kept in capped plastic tubes in the deep freeze (-20 °C) until analyzed (1-2 months). Serum PRL, FSH and LH level were determined by radioimmunoassay method using kits provided by (Amersham, Radio chemical center, Buckingham shire, U.K.)<sup>(4)</sup>. Statistical analysis was performed using unpaired t-test to compare the means of the serum PRL, LH and FSH of CRF patients with those of control group. All values are expressed as mean  $\pm$ SD.

## RESULTS

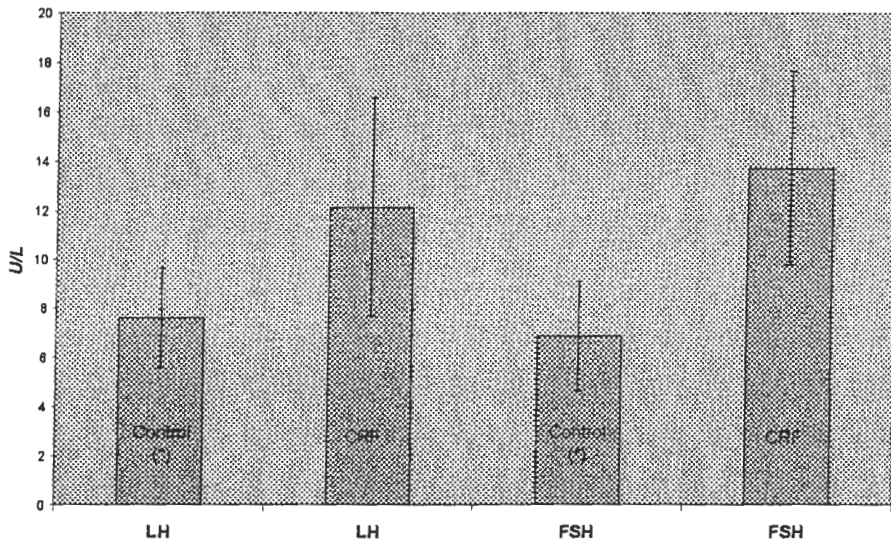
The study included 30 married uremic men who were on maintenance HD for more than two years. Three patients had primary infertility and eighteen patients had secondary infertility. The mean  $\pm$ SD of PRL, FSH and LH in patients with CRF and in control group are shown in (Table 1). Serum prolactin, FSH and LH were significantly higher ( $P < 0.0001$ ,  $P < 0.0001$  and  $P < 0.0001$ ) in patients with CRF in comparison to control group, (Figure 1, Figure 2).

**Table (1):** Mean  $\pm$ SD of serum prolactin (PRL), follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels in 30 uremic men on maintenance hemodialysis and control group.

	Mean $\pm$ SD		p-value
	Patients (n=30)	Control group (n=30)	
PRL mU/L	912.0 $\pm$ 308.0	213.6 $\pm$ 45.2	$P < 0.0001$
FSH U/L	13.5 $\pm$ 12.1	6.6 $\pm$ 2.7	$P < 0.0001$
LH U/L	12.5 $\pm$ 11.7	6.4 $\pm$ 2.1	$P < 0.0001$



**Figure (1):** Mean  $\pm$ SD of serum prolactin (PRL) in patients with chronic renal failure undergoing maintenance hemodialysis and control group. (Significantly differ in control group from respective values in patients with CRF).



**Figure (2):** Mean  $\pm$ SD of serum luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels in male patients with chronic renal failure undergoing maintenance hemodialysis and control group.

(\* significantly differ in control group from respective values in patients with CRF).

## DISCUSSION

The association of hyperprolactinemia and CRF has been reported in many studies<sup>(5,6)</sup> and it has been confirmed in the present study. Twenty six (86.7%) patients with CRF included in this study were found to have hyperprolactinemia. The mechanism of hyperprolactinemia in CRF patients seems to be multifactorial; increase in production rate is a major mechanism<sup>(7)</sup>, in addition to decrease in clearance rate<sup>(8)</sup>. A variety of conditions may contribute to increased PRL production like accumulation of uremic toxins<sup>(9)</sup>. These toxins might increase PRL secretion by suppressing the release of prolactin inhibitory hormone (PIH) by the hypothalamus or by decreasing the sensitivity of the pituitary lactotropes to PIH<sup>(10)</sup>.

The basal level of FSH was abnormally high in 12 (40%) patients with CRF included in this study. Follicle stimulating hormone plays an important role in spermatogenesis and high level of FSH had been observed in patients with testicular damage and impaired spermatogenesis caused by diseases other than CRF<sup>(11)</sup>. However, testicular damage with impaired spermatogenesis is a common complication of CRF. This might impair the negative feedback between the testis and anterior pituitary gland with a consequent increase in FSH production and secretion. High serum FSH is a usual indicator of primary hypogonadism and had been considered as

one of the main causes of infertility<sup>(12)</sup>. In fact 10 (83.3%) patients with elevated serum FSH had history of infertility in comparison to 7(38.9%) such patients with normal level FSH.

Seventeen (56.6%) of the patients with CRF included in this study had abnormally high serum LH level. The mechanism of this abnormality is not completely understood. Decreased testosterone production by the Leydig cells will impair the negative feedback control on gonadotrophin releasing hormone (GnRH) and consequently increase LH production<sup>(13)</sup>. A decrease in metabolic rate of LH may also contribute to such increase in serum level of LH in patients with CRF<sup>(14)</sup>. The incidence of infertility was less common in patients with normal serum hormones in comparison with those who had abnormally high serum hormones.

In summary the study shows a great deal of abnormally high serum level of PRL, FSH and LH in patients with CRF undergoing maintenance HD. These abnormalities may be attributed to decreased clearance rate of the hormone by the failed kidneys or due to increase the rate of production of these hormones or both of them. Furthermore, the results of this study revealed that these abnormalities have certain role in the pathogenesis of infertility encountered in patients with CRF.

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