Original Article

The role of sex hormones, waist circumference, BMI and Leptinemia in patients with acute renal failure.

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Summary:

Fac Med Baghdad 2008; Vol.50, No.2
Received Feb, 2008
Accepted April.2008

Background: Acute renal failure is characterized by impaired excretory endocrine homeostatic and metabolic functions of the kidneys.
Objective: The aim of this study is to look for the role of sex hormones, waist circumference and leptinemia in patients with acute renal failure.
Subjects and Methods: 55 subjects were involved in this study, 30 had acute renal failure and the remaining 25 subjects were normal healthy individuals who served as a control. The age range of the patients was between 25 and 45 years with a mean of 37±8.2 years.
Five mls of blood were withdrawn from each subject by vein puncture. Enzyme linked immuno assay (ELISA) was used for the measurement of serum leptin level.
Radio immuno assay (RIA) technique was used for the measurements of testosterone and estradiol levels.
Data were expressed as mean±SD. Results were evaluated using the student t-test for paired data. Conventional methods were used for the correlation and regression analyses.
Results: Patients with acute renal failure show a significant increase in leptin level, BMI and waist circumference than healthy group. On the other hand, testosterone level shows significant decrease while estradiol serum level shows a significant increase when compared with the healthy group in both genders although more significant in females.
Females with acute renal failure have significantly higher level of leptin than in males with acute renal failure as well as the anthropometrical measurements (BMI & waist circumference).
Conclusion: Increased level of serum leptin and estradiol in acute renal failure is a reflection of increased waist circumference of the patients and the effected renal parenchyma which make the ability of the kidney for biodegradation very poor. On the other hand testesteron has a significant effect on serum leptin levels as can be seen through its positive effect in males rather in females.

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Introduction:

Acute renal failure is a sudden, sharp decline in renal function as a result of an acute toxic or hypoxic insult to the kidneys, which impair their execratory, endocrine haemostatic and metabolic function[1]. The syndrome is usually

defined when the GFR is reduced below 10ml/min.
Patients with such a renal insufficiency usually show from the onset of the disease a pattern of hormonal changes resulting from complex disturbances at the hypothalamic-pituitary and gonadel level[2].

Leptin is among the hormones that usually biodegraded by the kidneys. It is an adipose derived polypeptide hormone, produced mainly by adiposites and its concentration usually correlate with body mass index and body fat content. Leptin and body weight are interrelated and a direct correlation has been found with normal renal function. Yet females are characterized significantly with higher serum leptin concentrations than males[3].
As the hormone biodegraded by the kidneys , therefore in chronic renal failure the level of leptin is increased tremendously[4].
The aim of the present work is to evaluate leptin serum level in patients with acute renal failure and to correlate the contribution of serum testosterone and astradiol concentrations with leptinemia in such patients. In order to shed some light on the mechanism of biodegradation of leptin by the kidneys in this disease.

Materials and methods:

A total of 55 subjects were involved in this study, 30 of them had acute renal failure all selected from patients attending Baghdad Teaching Hospital. The remaining 25 subjects were normal healthy individuals who served as a control. The age range of the patients was between 25 and 45 years with a mean of 37±8.2 years.
Sixteen of the patients were females. The remaining 14 patients were males. The age range of the control subjects was also between 25-45 years with a mean of 30±10.3 years, Table (1)
Five mls of blood were withdrawn from each subject by vein puncture. The blood was then transferred into plastic tubes, left for 2 hours before centrifugating them at 500rpm for 10 minutes to get as much serum as possible.
Enzyme linked immuno assay (ELISA) was used for the measurement of serum leptin level.
Radio immuno assay (RIA) technique was used for the measurements of testosterone and estradiol levels.
The radio immuno assay kits for the measurements of the mentioned parameters were obtained from DIOsorin, still waster, Minnesota USA.
Data were expressed as mean±SD. Results were evaluated using the student t-test for paired data. Conventional methods were used for the correlation and regression analyses.

Results:

Table (1) presents serum concentration of the examined hormones (leptin, testosterone and estradiol) and anthropometrical measurement (BMI & waist circumference for acute renal failure group and healthy group. Difference in mean values between acute renal failure and healthy group in both genders were assessed by student t-test.
Patients with acute renal failure show a significant increase in leptin level, BMI and waist circumference than healthy group. On the other hand, testosterone level shows significant decrease while estradiol serum level shows a significant increase when compared with the healthy group in both genders although more significant in females.
Females with acute renal failure have significantly higher level of leptin than in males with acute renal failure as well as the anthropometrical measurements (BMI & waist circumference).
Changes in the levels of leptin correlated positively with BMI, waist circumference and estadiol p,<0.05)leptin was also significantly correlated with testosterone ($p<0.05$) inversely, table 2.
Evaluation of the influence of sex steroids on leptin secretion independently from difference in body composition are summarized in table 3.
Females with acute renal failure have highly significant increase in leptin level.

Table(1)Mean values of anthropometrical measurement of studied hormones (leptin, testosterone and estradiol) in acute renal failure group compared to healthy group (±SD).

Studied parameters	Healthy group Mean ± SD		Acute renal failure Mean ± SD	
	Males	females	males	females
BMI kg/m	29.2 ±5.8	28.9±4.7	31.9 ± 3.0*	30.5±2.9*
Waist circumference cm	46.3 ± 5.1	40.1±4.8	55.8±4.3*	42.2±3.3*
Leptin ng/ml	5.6 ±1.9	13.6± 2.3	13.7±4.8*	27.4±8.4*
Testosterone ng/dl	31.5± 1.9	3.4±1.0	25.3±4.4*	1.4±0.7*
Estradiol pg/ml	12.8± 2.9	260±116	17.8±2.7*	321±27.5*

***p < 0.05**

Table 2: Rank correlation for leptin with BMI , waist circumference , estradiol and testosterone.

	Leptin hormone
BMI	0.40*
Waist circumference	0.50*
estradiol	0.49*
Testosterone	- 0.05*

*** p< 0.05**

Table 3 : Mean values of leptin level in serum of females with acute renal failure compared to males who have identical BMI (30.1 -30.8).

	Female with acute renal failure BMI kg/m^2 (30.1 – 30.8)	Male with acute renal failure BMI kg/m2 (30.1 -30.8)
Leptin ng/ml	27.5 ±8.4	13.7± 4.8**

*** p< 0.05**

Discussion :

Reduced renal function, directly or indirectly, seems to be closely related to cytokines elevation. Patients with decreased renal function already demonstrate signs of inflammation and the deterioration of renal function has been associated with a significant increase in serum level of such cytokines[5].
Leptin is an adipocyte-derived hormone that circulates in the serum in the free and bound form. Serum levels of leptin reflects the amount of energy stored in the adipose tissue. Short –term energy imbalance as well as serum levels of several cytokines and hormones influence circulating leptin levels. Leptin acts by binding to specific receptors in the hypothalamus to alter the expression of several neuropeptides that regulate neuroendocrine function and energy intake and expenditure[6] . The leptin-binding receptor protein is a large single membrane-spanning receptor[7] of the class 1 cytokine receptor family.
The findings of the present study is in disagreement with that of Ficek R,.et)[8] who suggests that patients with acute renal failure are characterized by normal plasma leptin concentration ,in contrast to the hemodialysed patients with chronic renal failure. This means that certain amounts of renal parenchyma in acute renal failure patients are affected.
Many studies hypothesized that the sexual dimorphism of leptin may be attributable to sex hormones, specifically estrogen and testosterone. Previous studies have identified the relationship between obesity and reproductive hormones, such as testosterone and estrogen[9,10].
Humans, as well as most of the anthropoid primates, exhibit pronounced sexual dimorphism in overall body size, with males typically being larger than females. However, there is also a pattern of sexual dimorphism in total fat accumulation [11] with females having a larger amount of fat relative to body weight than males [12]. Additionally, there is a marked sexual dimorphism in adipose tissue distribution [13].
In females, excess fat tends to be accumulated in the lower part of the body (e.g., hips and thighs), whereas in males it tends to accumulate on the upper part.(e.g., abdomen)[14].
Several studies have reported pronounced sexual dimorphism in fat accumulation and distribution as assessed through a variety of morphometric characters in a sample of Mexican Americans that have shown the sexual dimorphism exhibited in these traits which have a substantial genetic component[15].
Leptin possesses a sexual dimorphism, being higher in females than males of equivalent age and BMI even after correction for body fat mass[16]. The pulse amplitude of leptin is two to three times higher in females than in males and the expression rate of leptin mRNA in subcutaneous fat tissue is significantly higher in females than males. Moreover, in vitro, leptin secretion rate from males´ subcutaneous adipose tissue is 66% that of females´ [17]. At the same time leptin shows a negative correlated with androgen levels. Studies in vitro have explored the direct influence of leptin expression in the subcutaneous adipose tissue of males and females after a short exposure (24h) to andrgens and estrogens[16].
It seems that leptin expression in the adipose tissue is stimulated by estrogens. Suggesting that the sexual dimorphism of leptinemia in humans is estrogen receptor –dependent[18].
Another study showed a significant reduction in leptin concentration and in estradiol and progesterone concentrations in culture media of human granulose-lutein cells obtained from the follicular fluid of women undergoing in vitro fertilization. Suppressed estradiol secretion by human granulose-lutein cells did not modify the elevation of estradiol concentration. These studies indicate that a feedback loop might exist between estrogen and leptin. The estrogen induces directly and /or indirectly the secretion of leptin, while leptin inhibits estrogen synthesis[5].
Circumstantial evidence suggests that ovarian hormones might affect leptin production in a variable way[19]. Machinal-Quelin and colleagues[20] examined serum leptin levels and mRNA expression in rat adipose tissue during normal estrous cycles in rats and during artificial estrous cycles in ovariectomized rats. They found that estrogen induces increased serum leptin concentrations and leptin mRNA expression in adipose tissue.
These findings are in disagreement with J.Chudek and co-worker [21] who suggest that

testosterone and estradiol are minor contributors to leptinemia both in healthy subjects and haemodialysed patients . The main determination of leptinemia in these subjects is total body fat mass.

Conclusion:

Increased level of serum leptin and estradiol in acute renal failure is a reflection of increased waist circumference of the patients and the effected renal parenchyma which make the ability of the kidney for biodegradation very poor. On the other hand testosterone has a significant effect on serum leptin levels as can be seen through its positive effect in males rather in females.

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