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Research Article

EVALUATION OF SERUM PROLACTIN LEVEL IN CHRONIC KIDNEY DISEASE

NEHRU D, KANDASAMY S, CHANDRAMOULI RK, MUTHUMANI L*

Department of Internal Medicine, K.A.P.Viswanatham Government Medical College, Tiruchirapalli, Tamil Nadu, India.
Email: drmuthumani@yahoo.co.in

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ABSTRACT

Objective: To study the association between chronic kidney disease (CKD) and hyperprolactinemia.

Methods: The study was conducted in 50 patients with CKD admitted in K.A.P.Viswanatham Government Medical College/M.G.M. Government Hospital Tiruchirapalli, between August 2015 and December 2015, who were on maintenance dialysis. Fasting serum prolactin level was measured in them to assess the presence of hyperprolactinemia. It was a prospective descriptive cross-sectional study. Quantitative determination of serum prolactin was done by fully automated bidirectionally interfaced chemiluminescent immunoassay.

Results: Among the 50 CKD patients, 28 patients had raised serum prolactin levels. According to Statistical analysis of data using t-test, there is a significant association between increased serum prolactin levels and presence of CKD.

Conclusion: CKD is associated with increased serum levels of hormone prolactin (hyperprolactinemia).
- Hyperprolactinemia could be detected in 56% of patients with CKD

Keywords: Serum prolactin, Chronic kidney disease, Hypertension.

INTRODUCTION

Chronic kidney disease (CKD) is characterized by irreversible loss of renal function leading to excretory, metabolic, and synthetic failure culminating in accumulation of nonprotein nitrogenous substances and present with varied clinical manifestations.

Prolactin is a hormone secreted mainly by anterior pituitary gland. In addition, prolactin is also secreted by various tissues in the body. Main action of prolactin is to control breast development and lactation in women. The function of prolactin in men remains to be studied.

CKD is characterized by elevation of serum prolactin levels. Prolactin clearance is reduced in CKD, and its production is altered. Prolactin's biological activity is also increased [1].

In male CKD patients, hyperprolactinemia is associated with gynecomastia and sexual dysfunction. Hyperprolactinemia is also common among female CKD patients. It causes galactorrhea and gonadal disturbances with menstrual irregularities, commonly amenorrhea [2].

Several studies conducted recently are showing that prolactin may have several biologic actions that participate in the atherosclerotic process and leads to insulin resistance. It is also associated with endothelial dysfunction. Hyperprolactinemia is found in patients with essential hypertension [3], acute phase of coronary syndromes [4], during ischemic strokes [5], and transient ischemic attacks and in preeclampsia.

Elevated levels of serum prolactin which occurs in CKD may contribute to vascular derangements. This might lead to worse cardiovascular outcomes among CKD patients. This was undertaken as a prospective clinical and biochemical study of serum prolactin levels in CKD patients.

METHODS

The study was conducted in 50 patients with CKD admitted in K.A.P.Viswanatham Government Medical College/M.G.M. Government Hospital Tiruchirapalli, between August 2015 and December 2015.

The patients who fulfill the criteria for CKD and who were on maintenance dialysis were taken into the study. Fasting serum prolactin level was measured in them to assess the presence of hyperprolactinemia.

Criteria for CKD

1. Patients with established CKD on maintenance dialysis irrespective of etiology
2. Symptoms of uremia for 3 months or more
3. Elevated blood urea, serum creatinine, and decreased creatinine clearance
4. Ultrasound evidence for CKD:
   a. Bilateral contracted kidney size <8 cm in male and <7cm in females
   b. Poor corticomedullary differentiation
   c. Type II or III renal parenchymal changes
5. The following group of patients was excluded from my study
   a. Known patients of hypothyroidism
   b. Known patients of chronic liver disease
   c. Known patients with seizure disorder
   d. Those who are pregnant
   e. Patients with prolactinomas, acromegaly, and Cushing's disease
   f. Patients with craniopharyngioma, meningiomas, and sarcoidosis
   g. Patients with chest wall lesions, spinal cord lesions
   h. Patients with adrenal insufficiency
   i. Those patients on following medications:

Phenothiazines, haloperidol, monoamine oxidase inhibitors, tricyclic antidepressants, reserpine, methyldopa, metoclopramide, amoxapine, cocaine, and verapamil.

Detailed clinical history and examination were undertaken in all patients. Height and weight and blood pressure of all patients were recorded.

The following investigations were performed in them

Complete blood count, peripheral smear study, erythrocyte sedimentation rate, blood urea, serum creatinine, creatinine clearance, serum electrolytes, liver function test, lipid profile, urine

for albumin, sugar and deposits, and chest X-ray. Electrocardiography, ultrasonography abdomen, and fasting serum prolactin level.

After selecting the patients, about 5 ml of blood sample is collected in a nonheparinized bottle, and quantitative determination of serum prolactin was done by fully automated bidirectionally interfaced chemiluminescent immunoassay (CLIA).

The reference range for serum prolactin includes:

Normally menstruating females: 2.8-29.2 ng/ml
- Pregnant women: 9.7-208.5 ng/ml
- Postmenopausal women: 1.8-20.3 ng/ml
- Men: 2.1-17.7 ng/ml.

RESULTS

Among 50 patients, 46 patients were male patients and 4 patients were female patients. Among 50 patients with CKD, 29 years to 70 years. Among 50 patients with CKD, 7 patients were below 40 years of age, 18 patients were in the age group of 41-50 years, 17 patients were in the age group of 51-60 years, and 8 patients were 61 years and above. The duration of CKD in this study varied from 6 months to 8 years (Table 5).

The creatinine clearance varied from 4.77 to 46.0. Among the 50 CKD patients, 31 had creatinine clearance <15 ml/minutes, 18 patients had creatinine clearance 15-30 ml/minutes, and 1 patient had creatinine clearance in the range of 30-60 ml/minutes (Table 1).

Among the 50 patients with CKD, blood urea values varied from 45 mg/dl to 170 mg/dl (Table 2).

Among the CKD patients, serum creatinine values varied between 1.5 mg/dl and 18.4 mg/dl (Table 3).

In the 50 CKD patients studied all of them were found to be patients of systemic hypertension. Among the 50 CKD patients studied 19 patients were found to be present with type 2 diabetes mellitus. Among the 50 CKD patients, dyslipidemias were detected in 16 patients.

Serum prolactin

Serum prolactin level was measured for the 50 patients with CKD using fully automated bidirectionally interfaced CLIA. Among the 50 CKD patients, 28 patients had raised serum prolactin levels (Table 4).

According to statistical analysis of data using t-test, there is a significant association between increased serum prolactin levels and presence of CKD (Table 6).

As per the t-test, (Table 7) no significant association could be established between raised blood urea levels in patients with CKD and increased serum prolactin levels.

According to the results of *t*-test, (Table 8) no significant association could be established between serum creatinine levels in patients with CKD and increased serum prolactin levels among them.

As per the statistical analysis using *t*-test, (Table 9) there was no significant association between creatinine clearance in CKD patients and increased serum prolactin values in them.

DISCUSSION

In CKD patients, there are alterations in signal feedback mechanisms of various hormones in the body. In addition, alteration of hormonal production and elimination occurs [6].

Patients with CKD also suffer from various other conditions such as protein energy malnutrition, a state of chronic inflammation, multiple drug intake, and the presence of metabolic acidosis. Most importantly, there is a disturbance in the hypothalamic–pituitary–gonadal axis in patients with CKD [7].

One of the major endocrine abnormalities detected in patients with CKD is increased serum prolactin levels. Several studies have shown that serum prolactin levels remain elevated in patients with CKD. This increase occurs in both male and female patients with CKD. This is

Table 1: Creatinine clearance

Creatinine clearance ml/minutes	Chronic kidney disease stage	Number of respondents	Percentage
30-60	III	1	2
15-30	IV	18	36
<15	V	31	62

Table 2: Blood urea level

Blood urea (mg/dl)	Number of patients	Percentage
<60	4	8
60-80	9	18
80-100	9	18
100-120	15	30
120-140	8	16
>140	5	10

Table 3: Serum creatinine

Serum creatinine level	Number of patients	Percentage
<5	24	48
5-10	18	36
10-15	6	12
15-20	2	4

Table 4: Serum prolactin

Particulars	Number of respondents (n=50)	Percentage (100%)
Positive	28	56.0
Negative	22	44.0

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Item	Minimum	Maximum	Mean	Standard deviation
Age	29	70	51.46	9.197
Symptom duration	½	8	4.44	2.052
Urea	45.00	170.00	104.1200	30.30366
Creatinine	1.50	18.4	7.9500	11.79824
Creatinine clearance ml/mm	4.77	46.00	14.5244	8.68455
Serum prolactin (ng/ml)	4.27	126.59	33.2369	30.67783

Table 6: t-test, serum prolactin levels (ng/ml) significance of association between chronic kidney disease and increased serum prolactin levels

Hyperprolactinemia	Mean	Standard deviation	Statistical inference
Positive (n=28)	3.43	1.620	t=−4.704
Negative (n=22)	5.73	1.830	df=48
			0.000<0.05
			Significant

Table 7: t-test, serum prolactin levels (ng/ml), significance of association between blood urea levels in chronic kidney disease patients and increased serum prolactin levels

Urea	Mean	Standard deviation	Statistical inference
Positive (n=28) Negative (n=22)	111.1071 95.2273	31.86934 26.24778	t=1.887 df=48 0.065>0.05 Not significant

Table 8: t-test, serum prolactin levels (ng/ml), significance of association between serum creatinine levels and increased serum prolactin levels

Creatinine	Mean	Standard deviation	Statistical inference
Positive (n=28) Negative (n=22)	7.4250 8.6182	4.48757 17.26468	t=−0.352 df=48 0.727>0.05 Not significant

Table 9: t-test, serum prolactin (ng/ml), significance of association between creatinine clearance and increased serum prolactin levels in patients with chronic kidney disease

Creatinine clearance ml/min	Mean	Standard deviation	Statistical inference
Positive (n=28) Negative (n=22)	13.4182 15.9323	9.28529 7.83744	t=−1.016 df=48 0.315>0.05 Not significant

thought to be mainly due to reduced clearance by the kidneys. There is an alteration in the dopaminergic activity in patients with CKD. This leads to increased production of prolactin hormone. This also contributes to the increased prolactin levels seen in this group of patients.

A Similar study of evaluating serum prolactin levels in chronic renal failure patients, CKD patients on hemodialysis, and transplant recipients was conducted by Peces *et al*. In this study, Peces *et al*. conducted serum prolactin estimation in twelve patients with CKD who were on conservative line of treatment and thirty patients with CKD who were on hemodialysis, and nineteen patients with CKD who were post-transplant recipients with a functioning kidney [7].

At the end of their study, authors have shown that basal levels of serum prolactin remain elevated in patients with CKD. This increased serum levels of hormone prolactin was demonstrated in both CKD patients who were on conservative line of treatment and in CKD patients who were on hemodialysis. In their study, the authors also demonstrated that the elevated serum prolactin hormone level showed a blunted and delayed response to stimulation with TRH. In this study, Peces *et al*. also have shown that Serum prolactin levels remain normal in those CKD patients who have received a transplant with functioning kidney. In this study, authors have attributed the increased serum prolactin hormone levels to decreased renal catabolism and impaired hypothalamo–pituitary regulation.

A similar study of evaluating hyperprolactinemia and impaired pituitary response to suppression and stimulation in patients with CKD was conducted by V.S. Lim, S.C. Kathpalia, and L. Frohaman. In this study, authors also analyzed the reversibility of the above-mentioned abnormalities with renal transplantation. In this study, authors have demonstrated increased basal serum prolactin levels in patients with CKD. In this study, authors also have demonstrated that prolactin hormone showed a lack of responsiveness to suppressive as well as stimulatory agents. They attributed this lack of responsive ness to pathology at the pituitary either at the level of receptor binding or a post-receptor level [8].

Our study is consistent with results of above-mentioned studies in that in our study basal serum levels of hormone prolactin remained elevated in 56% of CKD patients. There was a statistically significant association between increased serum prolactin levels and presence of CKD.

CONCLUSION

- CKD is associated with increased serum levels of hormone prolactin (Hyperprolactinemia)
- Hyperprolactinemia could be detected in 56% of patients with CKD.

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