RESEARCH

A PROSPECTIVE STUDY ON THE EVALUATION OF SERUM PROLACTIN LEVELS IN CHRONIC KIDNEY DISEASE PATIENTS AND ITS CORRELATION WITH THE RISK OF CORONARY ARTERY DISEASE

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Received : 21/07/2022
Received in revised form : 12/09/2022
Accepted : 20/09/2022

Keywords:
Prolactin,
Hyperprolactinemia,
Coronary Artery Disease,
Chronic Kidney Disease.

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DOI: 10.47009/jamp.2022.4.4.120

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2022; 4 (4); 613-616

Abstract

Background: Prolactin clearance and production are changed in people with chronic renal disease, resulting in hyperprolactinemia. Furthermore, CKD is linked to an increased risk of coronary artery disease. New research reveals that prolactin plays a significant role in the atherosclerotic process. This study investigates the occurrence of hyperprolactinemia in chronic renal disease patients and the relationships between hyperprolactinemia and the incidence of coronary artery disease in these patients. **Materials and Methods:** A prospective, single-centre study was conducted in Madurai medical college hospital from January 2021 to June 2021. The study included 50 patients with chronic kidney disease who were already diagnosed with chronic kidney disease on medical management and dialysis treatment. The patients were examined for coronary artery disease using ECG and ECHO, and their fasting serum prolactin levels were tested to determine the existence of hyperprolactinemia. **Result:** In our analysis of 50 CKD patients, 45 were male, and four were female. No statistically significant gender of CKD patients is associated with serum protein levels. Twenty-eight exhibited hyperprolactinemia, accounting for approximately 56% of the study group. Furthermore, a significant relationship was discovered between elevated prolactin levels and CKD patients with dyslipidemia (p=0.015). Furthermore, 19 patients were diagnosed with CAHD; this is about 67.90%. Showed a significant association between Hyperprolactinemia in CKD patients & Occurrence of CAHD among them. **Conclusion:** Chronic kidney disease is related to elevated blood prolactin levels (hyperprolactinemia). As a result, we may conclude that hyperprolactinemia in chronic renal disease patients may be a risk factor for future risk of coronary artery disease.

INTRODUCTION

Chronic kidney disease (CKD) is becoming one of the world's most severe chronic risk factors for coronary heart disease epidemics, even in India. Management of CKD and its advanced state, end-stage renal disease (ESRD), clearly consumes a prominent aspect of health resources in much of the nation and is out of reach for the typical Indian. As a result, CKD prevention must become a priority for the medical community, government, and general population in any country, including India. CRF, also known as chronic kidney disease (CKD), is referred to as chronic kidney function failure, characterised as excessively increased serum creatinine for even more than three months or a measured glomerular filtration rate (GFR) of only about 60 ml per minute/1.73m2. It is frequently characterised by a gradual decrease in kidney function, needing renal replacement treatment (dialysis or transplantation). The end-stage renal disease occurs when a patient requires renal replacement treatment (ESRD).[1,2]

The anterior pituitary gland produces prolactin which is a hormone. Furthermore, numerous tissues in the body release prolactin. Prolactin's primary function in women is to regulate breast growth and breastfeeding. Prolactin's role in men is still being researched. The level of serum prolactin rises as the chronic kidney disease progresses. The rise of serum prolactin appears to be linked to a rise in serum creatinine.[3,4]

Hyperprolactinemia has been associated with sexual dysfunction in males with chronic renal illness. Hyperprolactinemia has been associated with libido loss. This may contribute to gynecomastia and sexual dysfunction in male CKD patients. In addition, gonadal abnormalities with monthly menstrual irregularities, mainly amenorrhoea noted in female CKD patients. Several recent investigations have revealed that prolactin may play a role in the atherosclerotic process through various biologic effects.[5] Hyperprolactinemia is linked to an increase in inflammatory processes, and an increase in prolactin levels in the bloodstream is linked to endothelial dysfunction. This also leads to the development of insulin resistance. Patients with essential hypertension often have hyperprolactinemia.[6]

In patients with acute coronary syndromes, ischemic stroke and transient ischemic attacks were also noted to have elevated serum prolactin levels during attacks. In addition, hyperprolactinemia is also found during eclampsia attacks. Heart failure in postpartum cardiomyopathy linked with elevated levels of serum prolactin. Many studies are showing this relationship. Recent data suggest that prolactin receptors exist in the plaques of atherosclerosis. The increase in the prolactin level is linked to an increased risk of coronary artery disease in men with erectile dysfunction.[7] The consequences of hyperprolactinemia in chronic kidney disease are not fully understood. Prolactin levels in the blood are high in chronic renal disease patients, which leads to vascular dysfunction. This might worsen and contribute to increased cardiovascular outcomes in CKD patients.[8]

AIM

To investigate the relationship between chronic kidney disease, hyperprolactinemia, and coronary artery disease incidence in CKD patients with hyperprolactinemia.

MATERIALS AND METHODS

A prospective, single-centre study was conducted on patients admitted to Madurai medical college hospital from January to June 2021. The study included 50 patients with chronic kidney disease. This study included patients who had already been diagnosed with chronic renal disease and received medical care and dialysis treatment. The patients were examined for coronary artery disease using ECG and ECHO, and their fasting blood prolactin levels were tested to determine the existence of hyperprolactinemia. Before participating, patients are given written informed permission.

Inclusion Criteria

The patient who fulfils the criteria for chronic kidney disease as Uremic symptoms for more than three months, Ultrasound evidence of chronic kidney disease. Serum creatinine, Elevated blood urea, and Decreased creatinine clearance.

Exclusion Criteria

Patients with hypothyroidism, chronic liver disease, Seizure disorder. Pregnancy, Acromegaly & Cushing's disease, Prolactinomas. Patients with Craniopharyngioma, Meningiomas, Sarcoidosis. Patients with chest wall lesions /surgeries, Spinal cord lesions. Patient with a history of galactorrhea. Patients with adrenal insufficiency. Patient on the following drugs is excluded from the study: Phenothiazines, Mono Amine Oxidase inhibitors, Chlorpromazine, Sulpiride, Metoclopramide, Tricyclic anti-depressants, Selective Serotonin reuptake inhibitors, Antiemetic agents, Opioid abuse, Cocaine abuse, Alpha Methyl Dopa.

Laboratory investigations are performed: Complete blood count, Serum creatinine, Blood urea, Creatinine clearance, Blood sugar fasting, Serum electrolytes, postprandial, Liver function tests, Lipid profile, Urine for albumin, Viral markers, Ultrasonography abdomen, ECG, ECHO, Fasting serum prolactin level. The data were statistically analysed using the SPSS software. In addition, many tests and methodologies were analysed, such as the t-test, Fisher exact test, Mann Whitney-U test, Chi-square test, etc.

RESULTS

Out of 50 patients, 45 were male, and five were female. No statistically significant gender of CKD patients is associated with serum prolactin levels. No statistically significant link exists between elevated prolactin levels and CKD patients with systemic hypertension. Similarly, no link was observed between elevated prolactin levels and CKD patients with type 2 diabetes mellitus. However, a significant link was observed between elevated prolactin levels and CKD patients with dyslipidemia ($p=0.015$). Elevated serum prolactin levels were related to CAD on ECG ($p=0.001$). In addition, increased serum prolactin levels correlated with ECHO indications of CAD ($p=0.001$).

No statistically significant difference exists between serum prolactin levels and CKD patients' age distribution p-value is 0.593. A link was observed between elevated serum prolactin levels, and chronic kidney disease p-value is <0.0001. Raised blood urea levels in CKD patients were not associated with elevated serum prolactin p-value is 0.743. No correlation was established between CKD patients' blood creatinine and prolactin levels p-value is 0.434. In addition, no correlation was established between CKD patients' blood creatinine clearance and prolactin levels p-value is 0.55. [Table 2]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 1: Distribution of Gender, SHTN, Type-II DM, Dyslipidemia, ECG evidence of CAD and ECG evidence of CAD.

Variable		Hyperprolactinemia negative	Percentage	Hyperprolactinemia positive	Percentage	p-value
Gender	Male	20	90.90%	25	89.30%	1
	Female	2	9.10%	3	10.70%	
SHTN		22	100%	28	100%	-
Type-II DM		13	59.10%	10	35.70%	0.153
Dyslipidemia		12	54.50%	5	17.90%	0.015*
ECG evidence of CAD		1	4.50%	19	67.90%	0.001*
2D ECHO evidence of CAD		1	4.50%	19	67.90%	0.001*

Table 2: The age distribution, Increased serum prolactin levels, urea, creatinine, and Cr. Cl levels in chronic kidney disease patients

Parameters		Hyperprolactinemia negative	Hyperprolactinemia positive	p-value
Age distribution	Mean	52.18	50.82	0.593
	Std. Deviation	10.773	6.875	
Serum prolactin	Mean	10.33	49.31	<0.0001
	Std. Deviation	3.94	29.07	
UREA	Mean	102.24	99.14	0.743
	Std. Deviation	23.29	30.88	
Creatinine	Mean	5.53	6.86	0.434
	Std. Deviation	2.59	4.31	
Creatinine Clearance ml/min	Mean	15.02	14.41	0.55
	Std. Deviation	8.27	10.34	

DISCUSSION

Our study included 50 patients with chronic kidney disease who were being managed medically and receiving dialysis therapy. The study has determined the relationship between blood prolactin levels and kidney diseases. Prolactin levels in our study blood were high in 56% of our study group. The remaining participants had normal serum prolactin levels. There is a link between elevated blood prolactin levels and chronic renal disease. In addition, one study shows hyperprolactinemia associated with essential hypertension.

Lim VS et al. conducted a similar study in individuals with chronic renal disease to investigate hyperprolactinemia and pituitary response to suppression and stimulation. The authors of this study also looked at whether renal transplantation anomalies mentioned above might be reversed. The authors of this study found that individuals with chronic renal illness have higher basal serum prolactin levels. The scientists also established that the Prolactin hormone is unresponsive to suppressive and stimulatory drugs in this investigation. This lack of response was linked to disease in the pituitary, either at the receptor binding level or at the post-receptor level.[9]

Peces R et al. studied serum prolactin levels in haemodialysis and transplant patients with chronic renal failure. Serum prolactin levels were evaluated in 12 patients receiving conservative therapy for chronic renal illness and 30 patients receiving dialysis for chronic renal disease. There are already 19 people who, due to kidney transplants, are healthy. After their research, the authors discovered that baseline levels of serum prolactin levels remain high. Both patients were on a conservative treatment plan for CKD, and the hemodialysis patients also received conservative therapy. The authors also investigated why TRH stimulation produced a minor reaction in their study. Hyperprolactinemia was also seen, with the authors attributing it to impaired renal clearance and altered hypothalamic-pituitary control.[10]

Sowers JR et al. investigated the role of prolactin in essential hypertension and Dopaminergic regulation of prolactin and blood pressure. Essential hypertension: a case with altered control central and peripheral dopaminergic systems appear to modify circadian variance in prolactin production and blood pressure, the researchers concluded. Furthermore, the increased prolactin levels also play a role in post-menopausal systemic hypertension.[11]

Akbari H et al. study shows that increased prolactin accelerates the process of arteriosclerosis by facilitating arterial stiffness. Moreover, atherogenesis is made worse by the inflammatory response that prolactin receptor signalling promotes inside the atherosclerotic plaque.[12]

Fifty patients with chronic kidney disease receiving medical and dialysis treatment were included in our study, and we calculated their blood prolactin levels. As a result, there was a statistically significant correlation between high blood prolactin levels and chronic kidney disease. Of these, 28 patients (or around 56%) had increased levels. Therefore, we did a further evaluation by using ECG and ECHO for those with elevated serum prolactin levels. The results of our study show that of the 28 patients with hyperprolactinemia, 19 had coronary artery heart disease, which is approximately 67.90%, and that there is a statistically significant association between hyperprolactinemia CKD patients and the development of coronary artery heart disease among them.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

CONCLUSION

Chronic kidney disease is related to elevated blood prolactin levels (hyperprolactinemia). Serum prolactin levels were elevated in 56% of our study of chronic kidney disease patients. Furthermore, when employing ECG and ECHO, around 67.90% of CKD patients with hyperprolactinemia demonstrated signs of Coronary Artery Heart Disease. As a result, we may suggest that hyperprolactinemia in chronic kidney disease patients may be a risk factor for future risk of Coronary Artery Heart Disease.

REFERENCES

1. Agarwal SK. Chronic kidney disease and its prevention in India. Kidney Int Suppl. 2005;(98):S41-5. doi: 10.1111/j.1523-1755.2005.09808.x.
2. Hou SH, Grossman S, Molitch ME. Hyperprolactinemia in patients with renal insufficiency and chronic renal failure requiring hemodialysis or chronic ambulatory peritoneal dialysis. Am J Kidney Dis. 1985;6(4):245-9. doi: 10.1016/s0272-6386(85)80181-5.
3. Carrero JJ, Kyriazis J, Sonmez A, Tzanakis I, Qureshi AR, Stenvinkel P, et al. Prolactin levels, endothelial dysfunction, and the risk of cardiovascular events and mortality in patients with CKD. Clin J Am Soc Nephrol. 2012;7(2):207-15. doi: 10.2215/CJN.06840711.
4. Yavuz D, Deyneli O, Akpinar I, Yildiz E, Gözü H, Sezgin O, et al. Endothelial function, insulin sensitivity and inflammatory markers in hyperprolactinemic pre-menopausal women. Eur J Endocrinol. 2003;149(3):187-93. doi: 10.1530/eje.0.1490187.
5. Stumpe KO, Kolloch R, Higuchi M, Krück F, Vetter H. Hyperprolactinaemia and antihypertensive effect of bromocriptine in essential hypertension. Identification of abnormal central dopamine control. Lancet. 1977;2(8031):211-4. doi: 10.1016/s0140-6736(77)92832-x.
6. Yavuz D, Topçu G, Ozener C, Akalin S, Sirikçi O. Macroprolactin does not contribute to elevated levels of prolactin in patients on renal replacement therapy. Clin Endocrinol (Oxf). 2005;63(5):520-4. doi: 10.1111/j.1365-2265.2005.02375.x.
7. McKenna TM, Woolf PD. Prolactin metabolic clearance and resistance to dopaminergic suppression in acute uremia. Endocrinology. 1985;116(5):2003-7. doi: 10.1210/endo-116-5-2003.
8. Caticha O, Norato DY, Tambascia MA, Santana A, Stephanou A, Sarlis NJ. Total body zinc depletion and its relationship to the development of hyperprolactinemia in chronic renal insufficiency. J Endocrinol Invest. 1996;19(7):441-8. doi: 10.1007/BF03349889.
9. Lim VS, Kathpalia SC, Frohman LA. Hyperprolactinemia and impaired pituitary response to suppression and stimulation in chronic renal failure: reversal after transplantation. J Clin Endocrinol Metab. 1979;48(1):101-7. doi: 10.1210/jcem-48-1-101.
10. Peces R, Horcajada C, López-Novoa JM, Frutos MA, Casado S, Hernando L. Hyperprolactinemia in chronic renal failure: impaired responsiveness to stimulation and suppression. Normalization after transplantation. Nephron. 1981;28(1):11-6. doi: 10.1159/000182087.
11. Sowers JR, Beck FW. Role of dopamine in the regulation of aldosterone and 18-hydroxycorticosterone secretion in man. J Endocrinol Invest. 1984;7(5):473-9. doi: 10.1007/BF03348453.
12. Ghoreshi ZA, Akbari H, Sharif-Zak M, Arefinia N, Abbasi-Jorjandi M, Asadikaram G. Recent findings on hyperprolactinemia and its pathological implications: a literature review. J Investig Med. 2022:jim-2022-002351. doi: 10.1136/jim-2022-002351.

ISSN (O): 2687-5365; ISSN (P): 2753-6556