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# Alteration of serum prolactin status in the patient with chronic kidney disease: a case control study

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**ABSTRACT:** Chronic kidney disease causes various types of endocrinal imbalance including the altered prolactin level. It causes altered circulatinghormonal concentration, altered peripheral metabolism, disturbed binding to carrier proteins &altered clearance of the hormone. There is increased basal level of serum prolactin in chronic kidney disease. However there is a paucity of Indian data in this respect. An observational case control study was performed among 100 patient with CKD (cases) & 100 healthy controls. There is significant increased level of serum prolactin (p value <0.001) among cases than controls. There is also statistically significant positive correlation has been found between serum prolactin & creatinine level. The diagnosis of hyperprolactinemia can be easily missed in the end stage kidney diseasepopulation because the symptoms of both the diseases overlap. In our study we have higher level of prolactin in study group. Clinician should pay attention this factor & there is a need to formulate the guideline of routine screening of serum prolactin level in CKD patients

**Keywords:** Chronic kidney disease, Hyperprolactinemia, Glomerular filtration rate, End stage renal disease

## I. INTRODUCTION:

Chronic kidney disease, also known as chronic renal failure defines the slow progressive irreversible loss of kidney function over a period of several years and it is one of the leading causes of death in world. [1] It is characterized by progressively decreased Glomerular filtration rate (GFR) which is as lower as less than 45 ml/min/1.73m$^2$& progressively increased levels of serum urea & creatinine. The kidney plays important role in producing and metabolizing a variety of hormones in our body. So when there is loss of kidney function the hormonal homeostasis is also affected. [2]

Prolactin is a protein hormone secreted from the lactotroph cells of anterior pituitary gland by stimulatory as well as inhibitory factors.Its biologic action in women is to control breast development and lactation. Prolactin is a hormone with important implications for more than 300 biological functions, for example immune functions, osmoregulation, sexual behaviour and reproduction, behaviour etc [3].Prolactin is involved in the regulation of several human reproductive functions mainly via the modulating effects of gonadotropins. Also Prolactin plays a critical role in human ovarian function supported by the observation that hyperprolactinemialeads to the development of amenorrhea and modifications of the luteal phase of the menstrual cycle [4]. Levels of circulating PRL between 3 and 15 µg/l are considered necessary for maintaining normal reproductive function, and levels below and above are associated with an increased rate of infertility. Even though hypoprolactinemia does not cause major clinical problems, a minimum concentration between 1 and 3 µg/l is thought to be necessary for the physiological regulation of ovarian function.

Prolactin has been shown to regulate fluid transport across cells in several different tissues such as mammary epithelial cells, intestinal epithelial cells, and amniotic cells, but relatively little information is available on its effects on renal ion transport and renal function [3,4]. Prolactin is a natriuretic hormone, which interacts with the renal dopamine system for its full effect. The natriuretic response of prolactin involves inhibition of proximal tubular $Na^+$, $K^+$-ATPase activity [5].

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Prolactin retention also leads to inhibition of gonadotropic hormone production, and testosterone deficiency in male CKD patients has indeed been linked to increased intima media thickness, atherosclerotic plaque occurrence, systemic inflammation, cardiovascular risk, and mortality.. Conversely, increased Prolactinemia could also be a consequence of decreased dopaminergic activity, which would in turn imply an increment in norepinephrine release and that may have adverse effects on endothelial function and on other organs, favoring myocardial hypertrophy, hypertension, and other cardiovascular comorbidities [6].

Hyperprolactinemia in CKD is the consequence of bothreduced renal clearance and increased production.CKD and progression toward ESRD expose patients to premature vascular disease and excess cardiovascular morbidity and mortality.Prolactin elevations occur in essential hypertension and during the acute phase of coronary syndromes, ischemic strokes, transient ischemic attacks , and preeclampsia playing a causative role in the heart failure that accompanies postpartum cardiomyopathy.Prolactin levels predicted major cardiovascular events in men with erectile dysfunction, and increased expression of prolactin receptors was found in advanced human atherosclerotic plaques [3,4,5].

## II. AIMS & OBJECTIVES:

The study was done to estimate the serum prolactin level in patients with chronic kidney disease and healthy volunteers and to evaluate their association.

## III. MATERIALS & METHODS:

This observational case control study was undertaken in the Department of Biochemistry in collaboration with the Department of Nephrology, NRS Medical College and Hospital, Kolkata, West Bengal, during the period from July 2019 to June 2020. Patients suffering from chronic kidney disease (diagnosed by serum urea and creatinine level) were taken as cases.Patients suffering from diabetes mellitus, malignancy, or having parathyroid abnormalities, pregnant women and who were on drugs like thyroxine, iodine, methimazole, propylthiouracil were excluded from the study. A total number of 100 patients suffering from chronic kidney disease were taken as cases & similar number of healthy controls were also included in the study. The approval of the study was taken from the Institutional Ethics Committee of NRS Medical College & Hospital.

Almost 5 ml of blood samples were collected from both cases &controls after8 to 10 hours of fasting, providing proper explanation and taking consents. Blood was collected aseptically in disposable syringes& immediately transferred into a plain vial to get clotted sample. After that the sample was centrifuged in 2500 rpm for 5 minutes. The serum was separated and was kept in aliquots and stored in minus twenty degree Centigrade (-20°C) refrigerator.

Serum urea and creatinine were measured by commercially available standardized kit by Berthelot and modified Jaffe's method in semi-autoanalyzer. Serum prolactin level was measured by ELISA method using standardized kit.

The data was tabulated and analysed using standardized statistical methods (SPSS20).

## IV. RESULTS:

In this study, 100 patients of chronic kidney disease and 100 healthy, age matched control subjects were studied. Biochemical parameters, namely urea, creatinine & serum prolactin were measured from the samples of the whole study population. The biochemical parameters of both patients and controls subjects are shown in table 1

| **Parameters** | **Case (n=100)** | **control(n=100)** |
|---|---|---|
| **Urea (in mg/dL) (MEAN** ± SD) | 161.81±56.38 | 34.37±8.45 |
| **Creatinine (in mg/dl) (MEAN±SD)** | 5.886±4.48 | 0.8970±0.1698 |
| **Prolactin (ng/dl) MEAN±SD** | 31.893±15.528 | 14.440±2.750 |

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Independent T tests were done between cases & control subjects taking the mean value of each parameter shown in table 2:

| Parameter | t value | p value |
|---|---|---|
| **UREA** | **12.26** | **<0.001** |
| **CREATININE** | **6.07** | **<0.001** |
| **PROLACTIN** | **6.078** | **<0.001** |

Value of serum urea, creatinine & prolactin were found to be significantly higher in cases than in controls. (p value < 0.005 was taken as statistically significant.)

Statistically significant positive correlation was found between serum creatinine and prolactin ( r value = 0.352 & p value = 0.019).

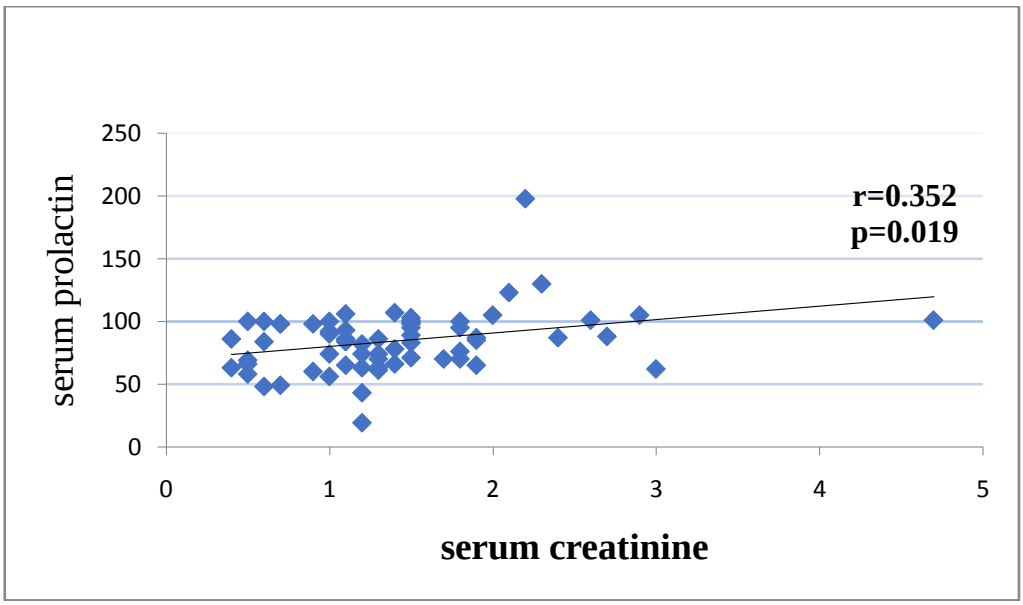


**Figure no- 1: Showing Correlation between serum creatinine and serum prolactin**.

## V. DISCUSSION:

The kidney has a central role in producing and metabolizing a variety of hormones. Gradual reduction of GFR & increased serum urea & creatinine level ultimately leads to end stage renal disease. [7] If chronic kidney disease ends in end stage renal disease the patient will not survive without dialysis.As the disease advances, it ultimately leads to uremia which is associated with multiple endocrine dysfunctions, including both alterations in signal-feedback mechanisms and in production, transport, metabolism, elimination and hormonal protein binding. The underlying mechanism for endocrine disturbances is very complex, modifying feedback mechanism and abnormal and altered metabolism, transport and synthesis of hormones.[8]

Hyperprolactinemia is very common in case of chronic renal failure patients ranging from 30% to 70%, due to mainly the consequence of reduced renal clearance but also increased production because of altered dopaminergic activity [9].The Cox analysis reveals that the risk of cardiovascular disease in non dialysed patients increased by 27% for each 10 ng/ml increment of prolactin and in hemodialysed patients these events increased by 12% which shows that prolactin may have several biological function which is related to artherosclrosis[10].The prolactin metabolizes in liver and kidney ,so the detoriation of kidney function elevates the level of prolactin. In SEPHADEX G-75 gel filtration of plasma from a chronic renal failure patient revealed that 94% of the immunoprecipitable radioactivity eluted in the

position of the PRL monomer. So nearly all endogenous plasma PRL immunoreactivity in chronic renal failure patients also eluted as the PRL monomer and disappearance of this endogenous PRL monomer during dopamine infusion. This leads to decreased dopamine effectiveness on PRL MCR and indicates that there is a interrelationship between hyperprolactinemia and chronic renal failure not only due to decreased PRL MCR but is primarily caused by increased secretion of prolactin [9,10].Peripheral conversion of oestrogen, thyroid hormones &catecholamines may elevate the prolactin secretion [10,11].It is believed that hyperprolactinemia may be compensatory mechanism counteracting hypercalcemia as prolactin is one of the factor stimulating 1,25(OH)2D3synthesis [11].Low T4 exhibit decrease negative feedback on hypo-thalamo-pituitary axis stimulates increased secretion of thyrotropin releasing hormone which can stimulate thyrotrophs and lactotrophs and increase the level of prolactin [12].

In our study,the mean prolactin level in patient 31.8930±15.52 and in control 14.44±2.75,state that serum prolactin level is significantly high in chronic renal failure patients than healthy individuals. In a study done byWallaschofski Het al it has been shown that hyperprolactinemia (PRL, >15 ng/ml plasma)was observed in 70% of 73 patientswith chronic renal failure (CRF) on maintenance hemodialysis. (13)The lack of response to dopamine infusion in CRF patients suggests a lactotroph resistance to dopamine which may be a significant factor in the etiology of hyperprolactinemia associated with this disease.So, hyperprolactinemia is common in patients with renal failure.

In our study statistically significant positive correlation has been found between serum prolactin & creatinine. Similar findings has also be found in the study done by Carrero JJ et al (27)

## VI. CONCLUSION:

Our study re-establishes the fact thatchronic renal failure patients haveincreased basal levels prolactin due to decreased renal catabolism and/or impaired hypothalamo- pituitary-regulation of prolactin secretion.

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**Limitation:**There were less number of individuals and most of the patients were from low socio economic status, so our subjects did not represent the whole population.

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