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Alteration of Thyroid Profile in Patients with Chronic Kidney Disease: A Case Control Study

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ABSTRACT: Chronic Kidney Disease affects thyroid function in multiple ways. It includes low circulating thyroid hormone concentration, altered peripheral hormone metabolism, disturbed binding to carrier proteins, reduced tissue thyroid hormone content, and increased iodine store in thyroid glands. Prevalence of hypothyroidism increased in CKD patients. However, there is a paucity of Indian data in this respect.
An observational case-control study was performed among 100 patients with CKD (cases) & 100 healthy controls. There is significant increase in TSH level in chronic renal failure patients ($p<0.001$) and changes in fT4 level was also found to be statically significant ($p<0.05$). there is also statistically significant decrease in serum fT3 in CKD patients ($p<0.001$). statistically significant positive correlation has found between TSH & fT4 level. The diagnosis of hypothyroidism can be easily missed in the end-stage kidney disease population, because the symptoms of chronic kidney disease and hypothyroidism overlap. In our study we have found high prevalence of hypothyroidism in study group. Clinicians should pay attention on this factor and there is a need to formulate guidelines to screen routinely for thyroid disorders in the chronic kidney disease population.

Keywords - Chronic kidney disease, Hypothyroidism, Thyroid stimulating hormone, Glomerular filtration rate

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/1.73m2& progressively increased levels of serum urea & creatinine. The kidney plays important role in producing and metabolizing a variety of hormones including the thyroid hormone in our body. So when there is loss of kidney function the hormonal homeostasis is also affected. [2]

A progressive reduction of renal function in chronic kidney disease disturbs in production & metabolism of thyroid hormones. The underlying pathophysiology of these derangements is likely multifactorial, involving iodine retention, altered serum protein binding capacity, systemic inflammation, malnutrition, metabolic acidosis and peripheral deiodinase activity. [3]

A progressive reduction in renal function is linked to alterations in thyroid hormone levels and metabolism, resulting in an especially high prevalence of subclinical hypothyroidism and the low T3 syndrome. This syndrome is mainly characterized by a decrease in total (T3) and free triiodothyronine (fT3) plasma concentration, whilst thyroid-stimulating hormone (TSH) and T4 remain in the normal range. [4] Subclinical hypothyroidism is also commonly observed in CKD patients. The prevalence of subclinical hypothyroidism increases consistently with decline in GFR. [5].

In chronic kidney disease the failure of peripheral conversion of T4 to T3 by deiodinase enzyme is decreased. CKD affects both hypothalamus pituitary thyroid axis and peripheral thyroid metabolism.As the kidney takes part in clearance of inorganic iodide through glomerular filtration,the serum iodine concentration is very high that leads to hypertrophic effect on the thyroid gland and block the pathway of thyroid hormone production. So, hypothyroidism occurs more frequently with increase prevalence of goiter [6].A decreased clearance of goitrogenic substances like aryl acid due to chronic renal failure may also accelerate the chance of goiter.Also, the increased level of phosphate, urea, creatinine, phenols may interrupt the binding between thyroid hormones and transporting protein (thyroid binding globulin protein and albumin) [9].In advanced stages of renal failure acidosis persists, which lowers the fT4 andfT3 concentrations and increase TSH level [7,8].

So, hypothyroidism whether it may be subclinical or overt is common in patient with chronic kidney disease as seen in various studies. But there is no such study done in recent past in our hospital population. This study was undertaken to estimate the serum TSH and Thyroid hormones in patients with chronic kidney disease and healthy volunteers and to evaluate their association.

II. 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 2016 to June 2017. 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. TSH, fT3, fT4 were measured by ELISA method using standardized kit.

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

III. RESULT

In this study, 100 patients of chronic kidney disease and 100 healthy, age matched control subjects were studied. Biochemical parameters, namely urea, creatinine, TSH, fT4& fT3 were measured from the samples of the whole study population. The biochemical parameters of both patients and controls subjects are shown in table 1. Independent T tests were done between cases & control subjects taking the mean value of each parameter shown in table1. Value of serum urea, creatinine, TSH & fT3 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 urea and fT3 & between creatinine and fT3.Statistically significant positive correlation was also found between TSH and fT4 (Table 2).

IV. FIGURES AND TABLES

Table1: comparison of biochemical parameters between cases & controls

Parameters	Case (n=100)	control(n=100)	t value	p value
Urea (in mg/dL)	161.81±56.38	34.37±8.45	12.26	<0.001
Creatinine (in mg/dl)	5.886±4.48	0.8970±0.1698	6.07	<0.001
TSH (ng/ml)	7.937±7.723	2.862±1.115	3.566	0.001
fT4 (ng/dl)	1.1802±0.5070	1.4060±0.3013	-2.18	0.032
fT3 (pg/ml)	1.665±0.477	2.487±0.5007	-7.06	<0.001

All data are expressed in **MEAN±SD,** Comparison done by Student t test

Table2: Correlation of serum urea & fT3 of cases &controls

Parameters compared	r value	P value
Serum urea & fT3	0.355	0.018
Serum creatinine & fT3	0.352	0.019
Serum TSH & fT4	0.297	0.017

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. [9] 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.[10]
Hypothyroidism is commonly associated with chronic kidney disease and its severity also progresses with progressive loss of kidney function as shown in various studies. Reduced glycosylation of TSH hormone, disturbed control of hypothalamus, diminished thyroid hormone production, defect in peripheral conversion, excretion& protein binding all contributes in the process.

In our study, the mean urea levels (mg/dl) in patients is 161.81±56.38 whereas the mean serum urea levels in control 34.37±8.45 mg/dl and the mean creatinine level in patients 5.883±4.48 and in in control 0.897±0.169.

In case of thyroid hormonal status, the mean TSH level in CKD patients and controls were7.937±7.72 µIU/ml and 2.862±1.11µIU/ml respectively. The fT4 level mean value in cases and control were 1.1802±0.507 ng/dl and 1.406±0.301ng/dl respectively .So there is a significant increase in TSH level in chronic renal failure patients ($p<0.001$) and the fT4 level was also found to be statistically significant ($p<0.032$).Besides, the mean fT3 level in CKD patient was 1.665±0.477 pg/dl and in control was 2.487±0.500 pg/dl, reveals that there is also statistically significant decrease in serum fT3 in CKD patients ($p<0.001$).

Subclinical hypothyroidism is quite common condition in persons with CKD. Montenegro J. et al showed that there is occurrence of hypothyroidism is seen in more than 55% of adults with chronic kidney disease. Kalogiros J.et al showed that the earliest and the most common thyroid dysfunction in CKD patients is low T3 level, especially total T3 than free T3.[4,11,7]

In our study we also have found that there is significant increase in TSH level in CKD patients but changes in fT4 level is not so significant. Beside this, there is an abrupt decrease in serum fT3 level in patients. The serum fT4 level does not decrease as much but the serum fT3 level falls because in CKD the peripheral conversion of fT4 to fT3 gets hampered. Although no recommendation available regarding the treatment of mild thyroid dysfunction in CKD patients but these abnormalities could represent a risk factor for cardiovascular disease and might also be implicated in kidney disease progression. [10,12]

VI. CONCLUSION

Our study reestablishes the occurrence of hypothyroidism in CKD patients and thus warrant more regular and vigilant checking of thyroid function in CKD patients and necessary intervention. However, there were a smaller number of individuals and most of the patients were from low socio-economic status, so our subjects did not represent the whole population. This may be considered as limitation of the study.

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