

A Study of Thyroid Profile with Chronic Kidney Disease in a tertiary care hospital in northern India

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ABSTRACT

Background

Chronic Kidney Disease (CKD) includes a spectrum of different patho-physiological events associated with abnormal renal functions and a progressive decrease in effective glomerular filtration rate. It is a condition defined by abnormalities of kidney structure or function for more than 3 months.

Objectives

The study aims to find out the status of thyroid dysfunction in patients with chronic kidney disease attending the Medicine OPD in Associated Hospital, GMC Rajouri and to find out the association between thyroid dysfunction and severity of the renal disease.

Material & methods

The study was conducted at GMC & Associated Hospital Rajouri in the Dept. of biochemistry in Collaboration with General Medicine department. The samples were collected from the dialysis unit. A total Number of 97 cases with CKD patients were included. A brief questionnaire was used for collecting the data like medical history, anthropometric data and other co-morbidities.

Results:-The study comprised of 97 CKD patients of different stages, with various demographical characteristics. Among which 64 (65%) were males and 33 (35%) females, which indicated that CKD is more common in males than females as per results. With respect to age, the results showed that as the age increases there is more probability of the disease as the age advances. (46.3% vs 29.0% vs 24.7%). Further it was found that staging of CKD disease, hypertension and diabetes had a significant association with the thyroid status of the patients ($X^2=14.81$, $p=0.000$), ($X^2=3.97$, $p=0.028$) and ($X^2=4.89$, $p=0.01$) respectively.

Conclusion

Hypertension is the main cause of CKD followed by diabetes and hypothyroidism is associated with the advancement of CKD.

Keywords: Chronic Kidney Disease, Hypothyroidism, Hypertension

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INTRODUCTION

Chronic Kidney Disease (CKD) includes a spectrum of different patho-physiological events associated with abnormal renal functions and a progressive decrease in effective glomerular filtration rate. It is a condition defined by abnormalities of kidney structure or function for more than 3 months.[1] CKD is a clinical syndrome which occurs due to irreversible loss of renal function leading to metabolic, endocrine, excretory and synthetic functions, resulting in accumulation of non-protein nitrogenous substances which lead to metabolic derangements and ends with distinct clinical manifestations. It is one of the steepest rising causes of death globally. Chronic kidney disease has become a global public health problem associated with high mortality and decreased quality of life: patients with CKD are at increased risk for progression to end stage renal disease which requires renal replacement therapy for long term survival. CKD prevalence as per a recent report, shows that stages 1 to 5 is 13.4% and 10.6% in stages 3 to 5 globally.[2] However, the reported prevalence of CKD varies widely amongst the studies because of high heterogeneity in population and number of patients studied. The burden of chronic kidney disease in India can't be assessed accurately. The approximate prevalence of CKD is 800 per million population and the incidence of end stage renal disease (ESRD) is 150-200, per million population CKD is a multifactorial pathological condition. However the most frequent causes of CKD remain type 2 diabetes and hypertension, besides these various other medical conditions can affect the kidneys and renal function deterioration can occur chronically over several years.[3] Hypertension is both a cause and a consequence of CKD, more than 50% of people who have elevated level of Serum Creatinine are hypertensive. Proteinuria, haematuria, abnormal blood tests of kidney function, and oedema are some of the signs and symptoms of CKD. When the renal function is strongly impaired, urine output is reduced, thereby leading to an increased amount of fluid in the body which can contribute to heart failure.[4] CKD affects the hypothalamus pituitary thyroid axis, causing thyroid dysfunction which subsequently affects thyroid hormone levels. Altered peripheral hormone metabolism and insufficient binding to carrier proteins causes reduced tissue thyroid hormone content and altered iodine storage in the

thyroid gland. Thus, in CKD thyroid hormone metabolism is impaired.[5] In view of the decreased thyroid function in CKD patients, we undertook the present study to find out the association between thyroid dysfunction and severity of the renal disease.

Aims and Objectives

The study aims to find out the status of thyroid dysfunction in patients with chronic kidney disease attending the medicine OPD in Associated Hospital, GMC Rajouri and to find out the association between thyroid dysfunction and severity of the renal disease.

Material and Methods

The study was conducted at Government Medical College & Associated Hospital Rajouri in the Department of Biochemistry in collaboration with General Medicine Department. The samples were collected from the dialysis unit. A total Number of 97 cases with CKD patients were included. A brief questionnaire was used for collecting the data like medical history, anthropometric data and other comorbidities. Duration of dialysis was also recorded. The patients having family history of thyroid disorder and who were on thyroid medications were excluded from the study. On consent of the patient blood samples were collected from those who agreed to participate in the study. Baseline biochemistry investigations were performed on Diatron-Pictus 500 automatic clinical chemistry analyser (Budapest, Hungary). Thyroid function test (TFT) was performed on VitrousEciQ immunodiagnostic system (Ortho Clinical Diagnostics, Rochester, NY, USA) auto analyser which worked on the principle of chemiluminescence immunoassay (CLIA). Here we used the normal range set by the GMC & Associated Hospital Rajouri, Central Laboratory Advance Biochemistry Section T₃(1.30 -13.10nmol/L), T₄ (66-181nmol/L) and TSH (0.27-4.20μIU/L). The statistical tools used were Minitab and Excel spread sheet, for ascertaining the association if any between Clinico-pathological parameters and CKD.

Results

The study comprised of 97 CKD patients with different stages, whose demographical characteristics are shown in (Table-1).

(TABLE 1): Demographical details of the study subjects

S.No.	Clinico-pathological Variable (n=97)	No. (%)
1.	Gender	
	Male	64 (65)
	Female	33 (35)
2.	Age	
	≤ 40	24 (24.7)
	40-60	29 (29)
	≥ 60	44 (46.3)
3.	Stage	
	Stage I	0
	Stage II	9 (9.2)
	Stage III	7 (7.2)
	Stage IV	4 (4.1)
	Stage V	8 (8.2)
	End Stage	69 (71.1)
4.	Cause:	
	Hypertension	55 (56.7)
	Diabetic Nephropathy	25 (25.7)
	Others	17 (17.5)
5.	Smoking Status:	
	Current Smoker	05 (5.1)
	Ex-Smoker	32 (32.9)
	Non-Smoker	60 (61.8)
6.	Cardiovascular Disease:	
	Yes	03 (3.4)
	No	94 (96.3)

Among which 64 (65%) were males and 33 (35%) females, which indicated that CKD is more common in males than females as per results. With respect to age, the results showed that as the age increases there is more probability of the disease. (46.3% vs 29.0% vs 24.7%). The study subjects were classified on the basis of stages of CKD, in which we have 0, 9, 7, 4, 8 and 69 number of patients in stages I (0.0%), II (9.2%), III (7.2%), IV (4.1%), V (8.24%) and end stage (ESRD) (71.1%) CKD patients respectively. The results suggest that the disease appears only when the disease has reached advanced stage (71.1% vs others). Regarding factors causing CKD, it was found hypertension was the most common cause and was present in 53 patients followed by diabetic nephropathy seen in 24 patients followed by others 17 (54.6% vs 24.7% vs 17.5%). When the study subjects were classified on smoking status, it was found that out of total patients 60 (61.8%) were the

non-smokers, 32 (32.9%) were having positive history of smoking and 5 (5.1%) were the current smokers, this indicate that in our study, smoking is not the cause for the development of CKD. Also in this study patients were also analysed for co-morbidities and among them cardiovascular disease which is having strong association with CKD was accessed, so when patients were analysed for co morbidity i.e cardiovascular disease, out of 97 Patients only 3 (3%) had cardiovascular disease (CVD) and 94 (96.9%) were not having CVD. After accessing thyroid stimulating hormone (TSH) levels in CKD patients, it was found that 57 (58.7%) were normal TSH levels i.e. euthyroid and elevated TSH levels i.e. hypothyroidism were found in 40 (41.3%) of patients. Also, it was observed that more males with CKD were affected with thyroid dysfunction as compared to female counter part 65.0% vs 35.0% respectively. (Table-2)

Table 2: Thyroid hormone status in as per Gender (n=97)

S.No.	Type	Male (N& %)	Female (N& %)	Total (N& %)
1.	Euthyroid	38(66)	19 (33.3)	57 (58.7)
2.	Hypothyroid	26(65)	14 (35)	40 (41.3)

When the association between thyroid status was compared with risk factors like age, sex, staging, cause of CKD and the smoking status, it was found

DISCUSSION

The present study was aimed to assess the prevalence of thyroid dysfunction in CKD patients attending Government Medical College and Associated Hospital Rajouri and to determine the association between thyroid dysfunction and severity of renal failure. A total of 97 patients were recruited for the study out of which 65% were male and only 34% were females which indicates that in our population there is also male predominance of CKD. More recent population-based, observational studies from the United States, Europe, and Japan, including several mass screening studies, have identified male sex as a predictor of poor kidney outcome [Babayev R, et al., 2013][Neugarten et al. 2000][6,7] assessed the risk of CKD progression in 68 cohort studies of patients with non-diabetic CKD and concluded that men progress to end-stage renal disease (ESRD) faster than women which is in concordance with our study. Also in this study, it was found that 41.3% of the patients had hypothyroidism and 58.7% were euthyroid and the prevalence of hypothyroidism was highest in the age group of 40-60 years. No significant association between the various age groups with CKD and thyroid status was found ($X^2=0.97$, $p=0.67$) but male predominance of CKD reflects the faster decline of GFR in males than females which is in accordance with reported studies men with chronic kidney disease (CKD) progress to end-stage CKD at a faster rate than women [Neugarten Jet al., 2000][7]. When the study subjects were classified

that staging of CKD disease, hypertension and diabetes had a significant association with the thyroid status of the patients.

based on age groups, it was found that 45% of cases were ≥ 60 years, possibly because of the deterioration of kidney function with age and inability of the body to maintain the kidney health as the age progresses. Chronic kidney disease (CKD) is common in the elderly [O'Hare AM et al., 2006].[8] Older age is a risk factor for the development of CKD [Fox CS, et al., 2004][9], most likely reflecting both lower mean levels of eGFR and higher rates of renal function loss in older compared with younger patients. Consistent with this possibility, among participants in the Baltimore Longitudinal Study of Aging without CKD, creatinine clearance declined at a higher rate among older compared with younger participants [Lindeman RD et al., 1985].[10]

With respect to stages of CKD, ESRD was found in 71% of the cases compared to the other stages of CKD. This shows the late presentation of the disease and absence or lack of screening tests on mass level for detection of early-stage CKD in our population. Also, it has been reported that in most

of the parts of the world CKD is detected in late stages by some accidental screening tests or routine check-ups. Also, kidney has a close relationship with thyroid gland so any disturbance or disease may lead to imbalance in kidney and thus kidney related diseases [Feinstein et al., 1982].[11] On comparing stages of CKD with the thyroid

disorder among the study samples it was found that out of 9 patients suffering from stage 2 CKD 66.6 % had hypothyroidism while as 33.3 % were normal. Among stage 3 patients who were 07 in number 57.1 % were found to have hypothyroid whereas 42.9 % were euthyroid. In the present sample, 04 patients were at stage 4 of CKD among whom 75 % were hypothyroid were as 25 % thyroid functioning was normal. Stage 5 witnessed 08 patients in all among whom majority of patients i.e. 87.5 % had hypothyroidism while only 12.5 % patient had no thyroid problem. As far as the end stage of the CKD was concerned there were a total of 69 patients out of which 29 % were suffering from hypothyroidism while as the majority i.e. 71 % had normal thyroid functioning. When comparing the stages of CKD with thyroid functioning, the result was found to be statically highly significant ($p < 0.000$) which is similar to the results found by [Ansari et al., 2023] [12] showing high TSH levels among subjects with different stages of CKD. TSH levels are often elevated in CKD in response to thyrotropin from pituitary as a result of uremic effect.

In another study the results indicate that the study population had hypothyroidism which is a common finding in CKD patients although statistically insignificant, [Mohammad Ali et al., 2014]. [13] According to [Connie M. Rhee et al 2016] [14] a growing body of evidence suggests that hypothyroidism is an individual risk factor for incident of CKD, its progression and higher death risk in kidney disease patients. Markedly, the positive cross-sectional association in our study between thyroid function and renal function with CKD could also be explained through the concept of reverse causativeness. Severe CKD commonly induces a hypothyroid state that exists in the absence of primary hypothalamic-pituitary-thyroid axis dysfunction.[15]

In this study we also found out that 56.7% of the CKD patients were hypertensive out of which 32.7% were hypothyroid which is in concordance with study conducted by [Keane et al 2005 and Yoshioka, 1987]. [16-17] Hypertension is one of the leading causes of CKD due to the deleterious effects of hypertension on kidney vasculature. Our findings also indicate the same results as hypertension appears to be the main cause of CKD in our case and is statistically significant. It has been

estimated that the prevalence of subclinical hypothyroidism ranges between 4 and 10% in the general population and it has been well observed that hypothyroidism (overt or clinical) increases with the increased risk for CVD.

Diabetes was the second most common cause for developing CKD in our study i.e. 25.7% were diabetic patients out of which 60% were hypothyroid, this was statistically significant, this is similar to the report according to CDC (Centre for disease control and prevention) 2022, which reveals that CKD is common in people with diabetes. [Dwyer, J. P. et al., 2012]. [18]

There were 32.8 % cases of smokers and 61.8% cases of non-smokers in this study out of which 40.5 % cases of CKD were hypothyroid with a habit of smoking and 41.6 % CKD cases with hypothyroid and non-smokers respectively. This is in contrast with the study conducted by [Gruppen, E.G et al., 2020] [19] which demonstrated lower TSH levels were associated with smoking. According to [Rabi Yacoub et al., 2010], [19] smoking increases the risk of CKD when compared to non-smokers, while in our study smokers having CKD with hypothyroidism did not have a statistically significant ($p = 0.6005$) difference when compared with non-smokers. So, it is highly recommended that screening for hypothyroidism in CKD patients should be considered in patients over all age groups, and that "aggressive case finding" should be considered in those at increased risk for hypothyroidism

LIMITATIONS

The present study had some limitations as this is the single center study so not all patients visit this center making the number of cases less. Besides, the patients who visit this center are in advanced stage of the disease. So, there could be some deviation in the results from other reported findings which could be reassessed or confirmed from a larger study including patients from all the stages and other centers of the healthcare in Rajouri in order to find some conclusive results. Furthermore, the population under study might differ from other populations/cases as we have different demographic, food and other cultural habits than rest of the populations which might also affect the results and observations, again warranting further studies on a larger number of patients.

CONCLUSION

As per the findings of the present study, Males are more prone to develop CKD in association with hypothyroidism than Females (65%,vs35%), However the association between the gender and

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the thyroid status was found to be non significant. Hypothyroidism is associated with the advancement of CKD i,e, ESRD. Hypertension is the main cause of CKD followed by diabetes in this study.

Table 3: Association of Thyroid status with study variables

S.No		Total (n=97)	Hypothyroid (n=40)	Euthyroid (n=57)	Chi square (p value)	
1.	Gender					
	Male	64	26	38	p=0.86	
	Female	33	14	19		
2.	Age					
	≤ 40	24	11	13	P=0.67	
	40-60	29	13	16		
	≥ 60	44	16	28		
		Stages of CKD				
		Stage I	0	0	0	p=0.000
		Stage II	9	6	3	
	Stage III	7	4	2		
	Stage IV	4	3	2		
	Stage V	8	7	1		
	End Stage	69	20	49		
4.	Cause of CKD					
	Hypertension	55	18	37	p=0.01	
	Diabetes	25	15	10		
	Others	17	7	10		
5.	Smoking Status					
	Current Smoker	05	01	04	p= 0.6005	
	Ex-Smoker	32	14	18		
	Non-Smoker	60	25	35		

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