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Research Article

High Prevalence of Subclinical Hypothyroidism in Chronic Kidney Disease patients caused by Diabetes and Hypertension at Nephrology & Urology Minia University Hospital

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Abstract

Background: Subclinical hypothyroidism (SCH) is becoming a major issue especially among patients with other chronic diseases like chronic kidney disease (CKD), hypertension (HTN), and diabetes mellitus (DM), but yet we have no solid data about the relationship between such diseases. **Objective:** our objective is to assess the prevalence of SCH among CKD patients and how it might be affected by the underlying cause of CKD at Nephrology & Urology Minia university hospital. **Methods:** 180 CKD patients aged between (18 and 60 years) all at stages (1 to 4) of CKD from outpatient clinics at our hospital were included. We investigated their thyroid and renal status by history, clinical examination, and laboratory tests. **Results:** we found a very high prevalence of SCH among CKD patients 48(26.7%) (P <0.0001). Causes of CKD significantly affected the prevalence of SCH: DM was associated with the highest prevalence of SCH (50%) (P <0.001), HTN was also associated with a rather high prevalence of SCH (40%) (P<0.001). While very low prevalence was found in obstructive uropathy, repeated urinary tract infection, congenital causes, G.N, lupus nephritis and others. **Conclusion:** SCH is highly prevalent among CKD patients especially when the underlying cause is DM or HTN.

Keywords: chronic diseases, prevalence, thyroid and renal status

Introduction

Over the past few decades SCH has proven to be of great significance as a risk factor for cardiovascular and neurological diseases especially in association with other chronic diseases [(1)]. On the other hand CKD is becoming a major health and economic problem which is responsible for huge numbers of mortalities and morbidities as well as a heavy economic burden all over the world [(2)]. Thyroid hormones are necessary for kidney development as well as the preservation of electrolytes and water balance, while the kidneys are involved in their metabolism and elimination [(3)]. Many previous studies have found relations between SCH and CKD progression and complications [(4-6)], but others found none [(7, 8)], the prevalence of SCH among CKD patients and how it might be affected by the presence of other chronic diseases is an area of great debate. The inter relation between SCH and other chronic diseases has been a topic for many recent studies, the understanding of such a relation is becoming a target for modern medicine.

Methods

This cross-sectional study included 180 patients of both sex from outpatient clinic of Nephrology unit at Nephrology and urology Minia university hospital over a period of 6 months from March to August 2022. Patients older than 60 years of age, younger than 18 years, pregnant women, critically ill patients,

stage 5 CKD, patients known to have any thyroid disease, and patients on thyroid specific medications were all excluded. All included patients underwent careful comprehensive history taking and physical examination including weight and height to calculate body mass index (BMI) by dividing the weight in kilograms by the height in square meters [9], then reviewing their previous laboratory and radiological data to establish CKD diagnosis and confirm the main underlying cause of CKD. Then Laboratory tests were performed on all patients including free thyroxine and free triiodothyronine (FT3 & FT4), thyroid stimulating hormone (TSH), and Serum creatinine & blood urea levels. CKD was defined on basis of persistent (>3 month) evident functional (proteinuria, hematuria) or anatomical abnormality and/or impaired estimate glomerular filtration rate (eGFR) [10], Euthyroidism was defined as a serum TSH and FT4 within the laboratory reference ranges of 0.26-4.2µlU/mL and 11.5-23.8 pmol/L respectively. Overt hypothyroidism was defined as decreased FT3 and FT4 below reference range with increased TSH level above reference range. Overt hyperthyroidism was defined as increased FT3 and FT4 above reference range with decreased TSH level below reference range. Subclinical hyperthyroidism was defined as normal FT4 while TSH level <0.26µIU/L, and SCH was defined as normal FT4 and TSH levels >4.2µlU/mL [11].

Ethical approval was obtained from the ethical committee of faculty of medicine, Minia University.

Statistical analysis: For quantitative variables, the data were presented as mean ± standard deviation (SD). While for qualitative variables, the numbers and percentages were used. For both quantitative and qualitative variables, the chi-square test and a general linear model were used to compare the data. SPSS Statistics version 25 was used for all statistical analyses. A P-value of less than 0.05 was deemed statistically significant for the results.

Results

The demographic data of the 180 participants are presented in Table (1). 106(58.9%) of participants were males while 74(41%) were females, with a mean age of (50.4 ± 7.05) years, most of our study group were overweight with a mean BMI of (25.3 ± 4.2). we had a large number of subjects with SCH among CKD patients 48(26.7%) (P<0.0001), while euthyroid patients were the majority 126(70%) of our studied patients, we also found a small percent of incidentally discovered overt hypothyroid 5(2.8%) and overt hyperthyroid 1(0.6%) patients Table (1).

DM and HTN were the leading causes of CKD with 48(26.7%) and 40(22.2%) of our patients respectively (P <0.001). Furthermore, the prevalence of other causes was as the following: Obstructive uropathy with 31(17.2%) patients, Cardiorenal syndrome, Congenital causes, repeated urinary tract infection, Glumerulo-nephritis (GN), and Lupus nephritis with 13(7.2%), 12(6.7%), 13(7.2%), 11(6.1%), and 9(5%) respectively, at last came other miscellaneous causes like idiopathic and surgical excision with 3(1.7%) of our patients Figure (1).

DM and HTN had the largest share of SCH cases with 40 (83.3%) of our SCH patients compared to just 8 (16.7%) in all other causes combined (P<0.0001) Table (2). CKD patients with DM or HTN as their main underling cause had a much higher prevalence of SCH with 50% and 40% respectively, cardiorenal syndrome had (23.1%), while other causes had lower percentages; Obstructive uropathy, Glumerulo-nephritis, congenital causes, repeated urinary tract infection (6.5%, 9.1% 8.3%, 7.7%) respectively. No cases of SCH were found in CKD caused by Lupus nephritis or other causes (P< 0.001) Table (3).

Table (1): Statistical distribution of Patients according to their demographic data and thyroid status.

		Studied cases (N=180)
Age (years)	**Range** **Mean ± SD**	18-60 years 50.4 ± 7.05
Gender	**Male (N,percent)** **Female (N,percent)**	106 (59%) 74 (41%)
BMI	**Mean ± SD**	25.3 ± 4.2
Thyroid state		
Normal thyroid function	**(N,percent)**	126(70.0%)
sub-clinical hypothyroidism	**(N,percent)**	48(26.7%)
overt hypothyroidism	**(N,percent)**	5(2.8%)
overt hyperthyroidism	**(N,percent)**	1(0.6%)

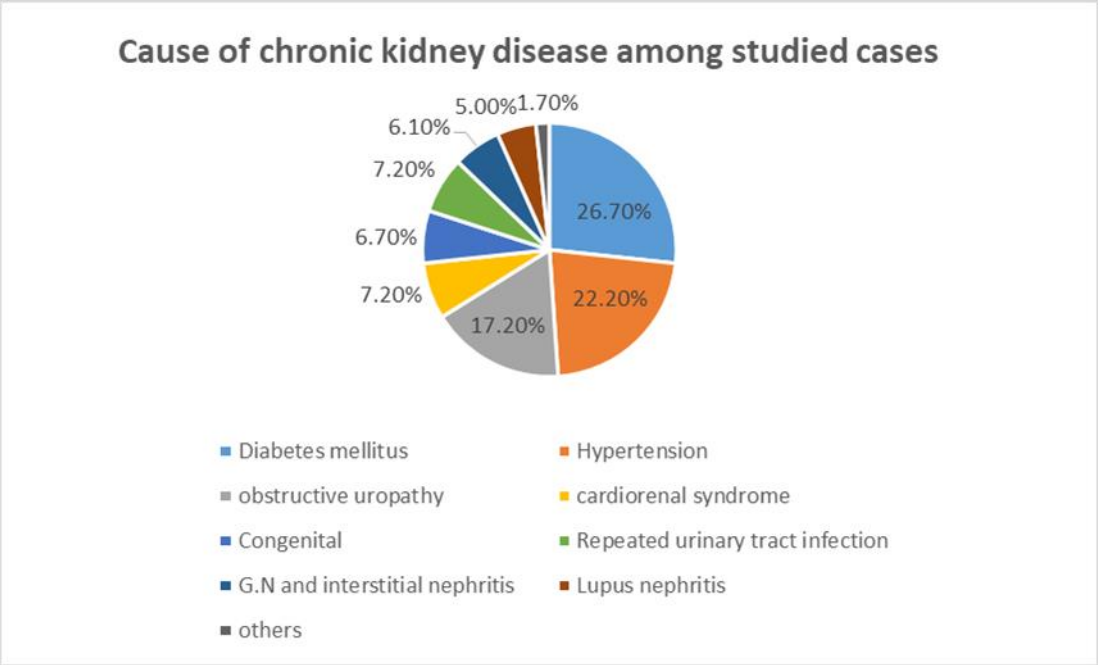

Figure (1): Cause of chronic kidney disease among studied cases.

Table (2): Cause of chronic kidney disease among studied cases according to their thyroid status.

Cause of CKD	Total number of cases	SCH cases	P-value
Diabetes mellitus	48	24(50%)	<0.001*
Hypertension	40	16(40%)	
obstructive uropathy	31	2(6.5%)	
cardiorenal syndrome	13	3(23.1%)	
Congenital causes	12	1(8.3%)	
Repeated urinary tract infection	13	1(7.7%)	
GN and interstitial nephritis	11	1(9.1%)	
Lupus nephritis	9	0(0%)	
Others	3	0(0%)	

Table (3): Cause of chronic kidney disease among studied cases and prevalence of SCH according to the cause.

Cause	Normal thyroid function (n =126)	sub-clinical hypothyroidism (n =48)	overt hypothyroidism (n =5)	overt hyperthyroidism (n =1)	p-value
Diabetes mellitus	24(19.0%)	24(50.0%)	0(0.0%)	0(0.0%)	<0.0001*
Hypertension	22(17.5%)	16(33.3%)	2(40.0%)	0(0.0%)	
obstructive uropathy	29(23.0%)	2(4.2%)	0(0.0%)	0(0.0%)	
cardiorenal syndrome	9(7.1%)	3(6.2%)	1(20.0%)	0(0.0%)	
Congenital	11(8.7%)	1(2.1%)	0(0.0%)	0(0.0%)	
Repeated urinary tract infection	12(9.5%)	1(2.1%)	0(0.0%)	0(0.0%)	
GN and interstitial nephritis	9(7.1%)	1(2.1%)	0(0.0%)	1(100.0%)	
Lupus nephritis	8(6.3%)	0(0.0%)	1(20.0%)	0(0.0%)	
Others	2(1.6%)	0(0.0%)	1(20.0%)	0(0.0%)	

Discussion

The general population prevalence of Subclinical Hypothyroidism (SCH) is about 10% [12]. In this cross-sectional study we found a very high prevalence of SCH in pre-dialysis chronic kidney disease (CKD) patients 48(26.7%) (P<0.0001). Many previous studies pointed to the link between chronic diseases such as CKD, Diabetes Mellitus (DM), and hypertension (HTN) and higher prevalence of SCH [13-15].

Previous studies suggested various explanations to the high prevalence of SCH among CKD patients as changes in the metabolism of iodine, a reduction in peripheral thyroid hormone sensitivity, reduction in thyroid gland response to TSH, or an increased incidence of autoimmune thyroiditis. However, the precise mechanisms behind this remain incompletely understood, and it is probable to have a complex etiology [14, 16]. Our results showed a high prevalence of SCH in diabetic and hypertensive CKD patients (50%, 40%) respectively (P<0.001). While patient with obstructive uropathy, GN, Congenital causes, repeated urinary tract infection, Lupus nephritis and other causes had a much lower percentage of SCH (6.5%, 9.1% 8.3%, 7.7%, 0%, 0%) respectively (P< 0.001).

Furthermore, DM and HTN combined had 40 (83.3%) of the total number of SCH in our study (P<0.0001). Some previous studies linked higher prevalence of SCH with aggressive diabetic nephropathy and uncontrolled HTN in CKD patients [14, 17]. The underlying mechanisms of the relation between SCH and other chronic diseases like DM or HTN have been studied extensively as they are very common in the general population. HTN was found to be a risk factor for SCH by inducing dyslipidemia and by augmenting possible auto immune thyroid destruction[15]. While DM might induce SCH by the impact of chronic hyperglycemia on peripheral T4 to T3 conversion, lipid profile, and the nocturnal peak of Thyrotropin releasing hormone (TRH) secretion. In addition, insulin is an anabolic hormone which increases FT4 levels while preventing the liver from converting T4 to T3, which lowers T3 levels [13, 18]. The concurrence of multiple chronic diseases (CKD, DM, HTN, dyslipidemia) may further increase the risk for SCH and even overt hypothyroidism. On the other hand SCH can aggravate CKD and accelerate its progression [5], SCH can lead to poor glycemic control by increasing peripheral resistance, in addition SCH is likely to progress to overt hypothyroidism in type 2 DM [19]. Also it is of great importance to point to SCH being linked to adverse cardiovascular effects and poor outcomes [1, 20].

So, we can say that SCH and chronic metabolic diseases are deeply interrelated especially CKD when the underlying cause is DM or HTN, and both can adversely affect each other. Early diagnosis and management of SCH among CKD patients is of great importance especially in diabetic and hypertensive patients.

Conclusion

Our findings showed a very high prevalence of Subclinical Hypothyroidism among pre-dialysis CKD patients caused by Diabetes and Hypertension.

Recommendations: Screening for SCH is mandatory in all CKD patients with diabetes and hypertension.

Conflicts of interest: No potential conflict of interest was reported by any of the authors.

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Ibrahim contributed through Data collection, analysis, interpretation, and statistical analysis of this manuscript.

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