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Association between Hypothyroidism and Chronic Kidney Disease in Patients with Type 2 Diabetes Mellitus in Saudi Community b based Hospital- A Retrospective Single Centre Study

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Abstract

Background and objective: The association between type 2 diabetes (T2DM) complicated with chronic kidney disease (CKD) and hypothyroidisms were not well studied. To estimate retrospectively the prevalence of hypothyroidism in patients with T2DM complicated with CKD in Saudi community based hospital.

Design: We analyzed retrospectively 1364 participants with T2DM whom are between the ages 20 to 96 years. All patients were from the population of the Primary health centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. All data were collected on the basis of a review of electronic medical data. Patients with Thyrotropin level (TSH) above the normal range of TSH for our laboratory reference, history of hypothyroidism and taking thyroid replacement therapy were included. Patient who are pregnant were excluded. All patients in the present study fulfilled the revised National Kidney Foundation criteria for the diagnosis of CKD.

Results: Out of 1286 subjects with T2DM, there were 346 cases (26.9%) male and 940 cases (73.1%) were female with mean age 55.4±12.3 and body mass index 31.8±6.3 kg/m^2. There were 53 cases (4.1%), 736 cases (57.2%) and 346 cases (26.9%) with CKD, hypertension and hypothyroidism respectively. The mean TSH and FT4 value was 4.2±8.0 mIU/l and

15.1±2.9 pmol/l respectively. Among cases of T2DM and CKD, there were 21 cases (39.6 %) with hypothyroidism, p=0.04. Regression analysis of odd ratio of risk factors for patients with T2DM and CKD with hypothyroidism showed that male gender, age, presence of hypothyroidism and HbA1c were associated with higher likely hood of CKD, (OR=11.5; 95% confidence interval [CI]=5.2, 25.6), p<0.0001), (OR=1.1; 95% CI=1.04, 1.1), p=0.004), (OR=4.4; 95% CI=2.1, 9.1), p<0.0001) and (OR=1.2; 95% CI=1.04, 1.4), p=0.01) respectively. Hypothyroidism with CKD was more prevalent in the seventh decade (17%). Prevalence of hypothyroidism was more prevalent across all age groups and significantly more prevalent in males as compared to females in the sixth (1.7% vs. 0.3%) and seventh (0.9% vs. 0.2%) decades.

Conclusion: We conclude that despite the limitations of this hospital-based retrospective study, hypothyroidism is highly prevalent in cohort of Saudis with CKD and T2DM. The majority of our patients with primary hypothyroidism in our finding were predominantly males. These two observations remain to be validated by population-based studies. In the absence of registry data, larger cooperative studies involving diverse population samples from multiple centers could help to provide further information on the true frequency nationally.

Keywords: Chronic Kidney Disease; Hypothyroidism; Type 2 Diabetes; Saudi Arabia

Introduction

Hypothyroidism has increased recently and is considered the commonest endocrine diseases [1]. Diabetes Mellitus is the commonest endocrine disorder, leading cause of death worldwide [2]. Saudi Arabia is the seventh of the top ten countries in terms of the prevalence of diabetes among the adult population aged 20-79 years [3].

Despite the growing literature about other metabolic and hormonal abnormalities that begin at much milder degrees of renal insufficiency, little is known about thyroid abnormalities or related adaptations in persons with chronic kidney disease (CKD) [4].

While numerous contributing factors have been suggested, including altered iodine metabolism and autoimmune thyroiditis, the exact mechanisms remain unclear. One previous study has examined the prevalence of hypothyroidism among patients with CKD. Among a small group of patients with diabetic and nondiabetic nephropathy, 24% of study subjects had overt or subclinical hypothyroidism, with a higher prevalence among patients with diabetes [5]. Lo, et al. [6] reported a prevalence of hypothyroidism of 23.1% in CKD patients. In another study, clinically apparent hypothyroidisms have been reported to occur in 18-20% of patients with CKD not requiring renal replacement therapy [7].

Thus, the present study was conducted to find out the relationship between CKD and hypothyroidism in patients with type 2 diabetes (T2DM) in a cohort of Saudi population.

Methods

We analyzed retrospectively 1286 participants whom are between the ages 20 to 96 years. All patients were from the population of the Primary health centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. All data were collected on the basis of a review of electronic medical data. Patients with Thyrotropin level (TSH) above the normal range of TSH for our laboratory reference, history of hypothyroidism and taking thyroid replacement therapy were included. Patient who are pregnant were excluded. The reference range values of TSH 0.22-4.2 MIU/L, Free T4 12.0-22.0 pmol/L. Participants were defined as having T2DM according to self-report, clinical reports, use of antidiabetic agents and HbA1c (≥6.5) [8]. HbA1c was expressed as percentage. High performance liquid chromatography was used. HTN was defined when the systolic blood pressure was ≥130 mm Hg and/or diastolic blood pressure was ≥85 mm Hg in addition to receiving any medication for hypertension [9]. All patients in the present study fulfilled the revised National Kidney Foundation criteria for the diagnosis of CKD [10]. The independent relationship between the stratified risk factors and the odds ratio of having albuminuria were analyzed using logistic regression. The

total number of cohort were separated on basis of age values into five groups: <50 years, 50-59 years, 60-69 years, 70-79 years and ≥80 years.

Statistical Analysis

Continuous variables were described using means and Standard Deviations. Univariate analysis of baseline demography both between groups, were accomplished using unpaired t-test and Chi square test were used for categorical data comparison. Regression analysis was performed to assess for odd ratio (OR). P value <0.05 indicates significance. The statistical analysis was conducted with SPSS version 22.0 for Windows.

Results

Out of 1286 subjects with T2DM included, there were 346 cases (26.9%) male and 940 cases (73.1%) were female with mean age 55.4±12.3 and BMI 31.8±6.3 kg/m^2, Table 1. There were 53 cases (4.1%), 736 cases (57.2 %) and 346 cases (26.9%) with CKD, HTN and hypothyroidism respectively. The mean TSH and FT4 value was 4.2±8.0 mIU/l and 15.1±2.9 pmol/l respectively. Among cases of T2DM and CKD, there were 21 cases (39.6%) with hypothyroidism, p=0.04, Table 2. Regression analysis of odd ratio of risk factors for patients with T2DM and CKD with hypothyroidism showed that male gender, age, presence of hypothyroidism and HbA1c were associated with higher likely hood of CKD, (OR=11.5; 95% confidence interval [CI]=5.2, 25.6), p<0.0001), (OR=1.1; 95% CI=1.04, 1.1), p=0.004), (OR=4.4; 95% CI=2.1, 9.1), p<0.0001) and (OR=1.2; 95% CI=1.04, 1.4), p=0.01) respectively, Table 3. Hypothyroidism with CKD was more prevalent in the seventh decade (17%), Figure 1. Prevalence of hypothyroidism was more prevalent across all age groups and significantly more prevalent in males as compared to females in the sixth (1.7% vs. 0.3%) and seventh (0.9% vs. 0.2%) decades, (Figure 2).

Parameters		Total (1286)
Age (years)		55.4 ±12.3
Gender	Male	346 (26.9)
	Female	940 (73.1)
Body mass index (kg/m^2)		31.8 ±6.3
Hypertension		736 (57.2)
Chronic kidney disease		53 (4.1)
Hypothyroidsm		346 (26.9)
HbA1c		8.1 ±2.2
TSH (mIU/l)		4.2 ±8.0
FT4 (pmol/l)		15.1 ±2.9
Serum creatinine (µmol/L)		69.2 ±26.1

Table 1: Base line characteristic of patients with type 2 diabetes [mean±standard deviation or number (%)].

Parameters		Chronic kidney disease		P value
		Present	Absent	
		53 (4.1)	1233 (95.9)	
Age (years)		64.5 ±10.7	55.0 ±12.2	<0.0001
Gender	Male	36 (67.9)	320 (25.1)	<0.0001
	Female	17 (32.1)	923 (74.9)	
Body mass index (kg/m^2)		30.4 ±6.9	31.9 ±6.3	0.1
Hypertension		44 (83.0)	692 (56.1)	<0.0001
Hypothyroidism		21 (39.6)	325 (26.4)	0.04
HbA1c		9.2 ±2.2	8.1 ±2.2	<0.0001
TSH (mIU/l)		4.0 ±3.5	4.2 ±8.1	0.9
FT4 (pmol/l)		15.1 ±2.8	15.1 ±2.9	0.9
Serum creatinine (µmol/L)		145.4 ±47.9	66.0 ±18.8	<0.0001

Table 2: Comparison between patients with type 2 diabetes with and without chronic kidney disease [mean±standard deviation or number (%)].

Parameters	Odd Ratio	P value
Male gender	11.5 (5.2-25.6)	<0.0001
Age (years)	1.1 (1.04-1.1)	0.004
Hypertension	2.2 (0.98-1.1)	0.06
Hypothyroidism	4.4 (2.1-9.1)	<0.0001
HbA1c	1.2 (1.04-1.4)	0.01

Table 3: Regression analysis for odd ratio of risk factors for patients with type 2 diabetes and chronic kidney disease.

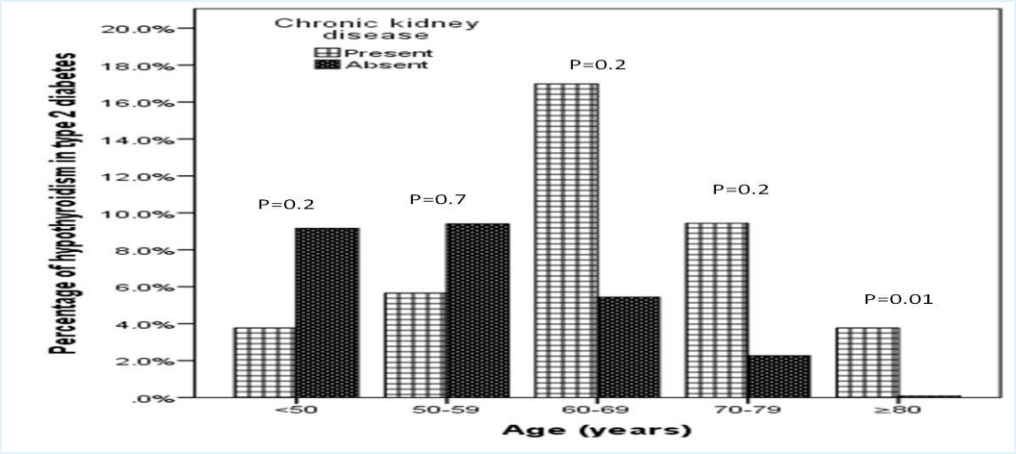

Figure 1: Age category groups and the frequency of hypothyroidism in patients with type 2 diabetes with and without chronic kidney disease.

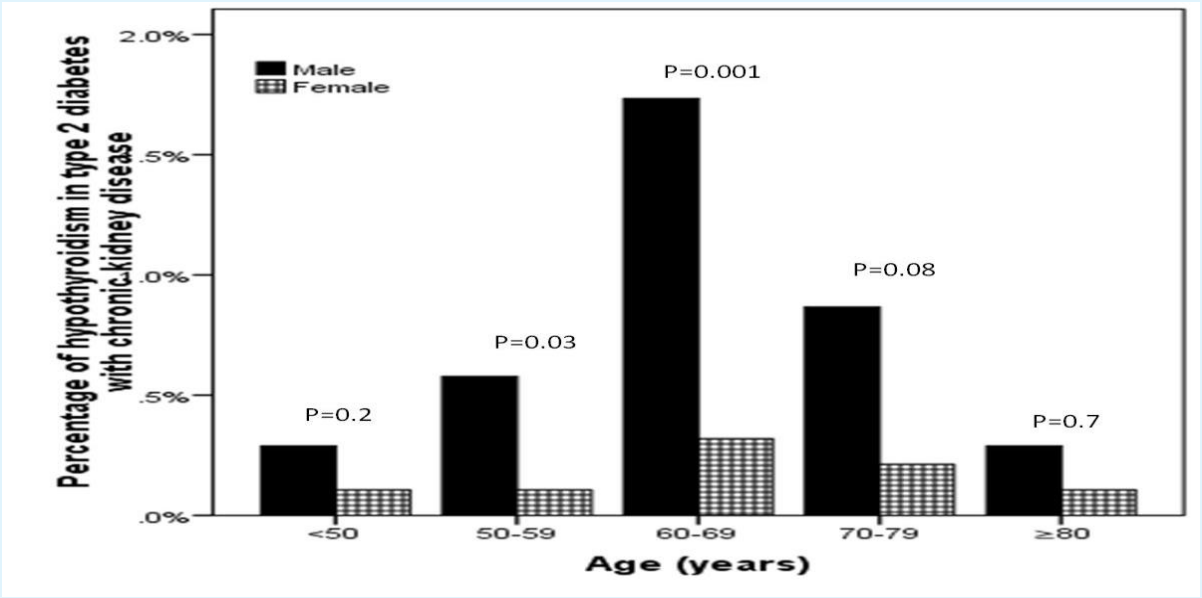

Figure 2: Age category groups and the frequency of hypothyroidism in patients with type 2 diabetes with and without chronic kidney disease in correlation to gender.

Discussion

Among a nationally representative sample of Saudis, we found an increased prevalence of hypothyroidism in persons with CKD, independent of age and gender. The current study revealed that hypothyroidism in patients with T2DM complicated by CKD was found in 39.6 %. To our knowledge, this is the first national and the largest study to explore the association between hypothyroidism and CKD in T2DM population. Chronic kidney disease is a worldwide public health problem. They are the 12th cause of death and 17th cause of disability respectively [11]. The association between diabetes and thyroid disease is well known. Thyroid diseases are also common in the general population. Most reports documenting hypothyroidism with renal impairment have described patients with unexplained worsening of pre-existing renal disease of an alternative aetiology. Recent epidemiological studies, identifying a high prevalence of thyroid dysfunction amongst patients with renal impairment, lend a new importance to the phenomenon of reversible hypothyroidism-induced renal impairment. Clinically-apparent hypothyroidism occur in 18–20% of patients with chronic kidney disease not requiring renal replacement therapy, with the prevalence rising as the degree of renal impairment worsens [6,7].

The causal relationship between hypothyroidism and CKD is also uncertain. Increased prevalence of goiter and thyroid gland volume have been reported in patients with end-stage renal disease (ESRD), and it has been suggested that primary hypothyroidism may be more common in patients with ESRD compared with the general population [12-14]. Despite the growing literature about other metabolic and hormonal abnormalities that begin at much milder degrees of renal insufficiency, little is known about thyroid abnormalities or related adaptations in persons with CKD who do not require maintenance dialysis [4]. Although numerous hypothesis for contributing factors, like altered iodine metabolism, decreased peripheral sensitivity to hormones, and autoimmune thyroiditis, the exact underlying mechanisms linking advanced CKD and primary thyroid dysfunction remain unclear [7]. One previous study has examined the prevalence of hypothyroidism among patients with CKD not requiring dialysis. Among a small group of patients with diabetic and nondiabetic nephropathy, 24% of study subjects had overt or subclinical hypothyroidism, with a higher prevalence among patients with diabetes [5].

The present study showed that the prevalence of hypothyroidism in patients with T2DM complicated by CKD was more in males (61.9%) as compared to females (38.1%), $p<0.0001$. This is consistent with the study of Shantha, et al. which showed prevalence of disease was higher in males (73.5%) as compared to females (26.5%) out of 137 ESRD patients and in contrast to the study showed that the prevalence of hypothyroidism was 25%, which was more in females (52%) as compared to males (48%) [15,16].

Hypothyroidism occurs in all ages, but it is usually more prevalent, in both community- and hospital-based populations, in older people in their sixth and seventh decades [17,18]. The present study showed that the prevalence of hypothyroidism was highest in age group of 60-69 years which older than others. [15] The risk of CKD, increased by 4.4 for hypothyroidism as compared to euthyroidism, which remained significant after adjustment for other potential risk factors of CKD.

We aimed to identify the frequency of hypothyroidism in patients with T2DM complicated with CKD in primary health care setting. Furthermore, due to the retrospective nature of this study, the observed population reflects a selected yet comprehensive group of patients rather than the general population. Our study could be limited by the question of clustering of cases within the study region and the effect that might have on our estimates, in addition, the current study population may appear limited in size and therefore may underestimate the true frequency of hypothyroidism in patients with T2DM complicated with CKD. In addition, the study shares the limitations of all retrospective studies.

We conclude that despite the limitations of this hospital-based retrospective study, hypothyroidism is highly prevalent in cohort of Saudis with CKD and T2DM. The majority of our patients with primary hypothyroidism in our finding were predominantly males. These two observations remain to be validated by population-based studies. In the absence of registry data, larger cooperative studies involving diverse population samples from multiple centers could help to provide further information on the true frequency nationally.

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Conflict of Interests

The authors declare no conflict of interests.

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