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Association between Hypothyroidism and Albuminuria in Patients with Type 2 Diabetes Mellitus in Saudi Community based Hospital. A Retrospective Single Centre Study

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Abstract

Background and Objective: The association between Type 2 Diabetes (T2DM) complicated with albuminuria and hypothyroidism were not well studied. To estimate retrospectively the prevalence of hypothyroidism in patients with T2DM complicated with albuminuria 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. Albuminuria was defined as AER ≥ 30 g/min in overnight urine collections.

Results: Out of the initial screening of 6023 subjects, 1364 subjects with T2DM were included. There were 861 (22.9%) male and 2899 (77.1%) were female with mean age 55.9 ± 12.4 and BMI 31.8 ± 6.3 kg/m^2. There were 515 (37.8%), 791 (58.0%) and 423 (31.0%) with albuminuria, Hypertension (HTN) and hypothyroidism respectively. The mean TSH and FT4 value was 4.4 ± 8.3 mIU/l and 15.1 ± 2.9 pmol/l respectively. Among cases of T2DM and albuminuria, there were 185 (35.9%) with hypothyroidism. Regression analysis of odd ratio of risk factors for patients with type 2 diabetes and albuminuria with hypothyroidism showed that female gender, HTN, presence of hypothyroidism and HbA1c were associated with higher likely hood of albuminuria, (OR=1.8; 95% Confidence Interval [CI]=1.4, 2.4), p<0.0001), (OR=2.4; 95% CI=1.8, 3.1), p<0.0001), (OR=1.8; 95% CI=1.3, 2.3), p<0.0001) and (OR=1.2; 95% CI=1.1, 1.3), p<0.0001) respectively. Cases with hypothyroidism were nonsignificantly showed no differences in HbA1c than cases with no hypothyroidism, 7.9 ± 2.3 vs. 8.1 ± 2.1 respectively, p=0.2. Hypothyroidsm with albuminuria was more prevalent in the seventh decade (32%). Hypothyroidsm was nonsignificantly more prevalent in females in the sixth decade and male in the seventh decade.

Conclusion: We conclude that despite the limitations of this hospital-based retrospective study, hypothyroidism is highly prevalent in cohort of Saudis with albuminuria and T2DM. The majority of our patients with primary hypothyroidism in our finding were predominantly females. 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: Albuminuria; Hypothyroidism; Type 2 diabetes; Saudi Arabia

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Introduction

Thyroid gland is one of the important organs in human body and the burden of thyroid diseases in the general population [1,2]. Hypothyroidism has increased recently and is considered the commonest endocrine diseases [3]. Diabetes Mellitus is the commonest endocrine disorder, leading cause of death worldwide [4]. Saudi Arabia is the seventh of the top ten countries in terms of the prevalence of diabetes among the adult population aged 20 to 79 years [5].

Given that diabetic nephropathy is the primary indication for hemodialysis in Saudi Arabia, prevention of disease progression is necessary to reduce the number of patients on dialysis. 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 [6,7]. In addition, thyroid hormone abnormalities have been reported among euthyroid patients with ESRD, including reduced total and free triiodothyronine and thyroxine levels [8]. Reasons for these latter findings are unclear, but it has been postulated to be due, at least in part, to an adaptive response to chronic nonthyroidal illness, unresolved uremia, and protein malnutrition [9].

Sporadic cases of reversible reduced glomerular filtration rate secondary to overt hypothyroidism have been reported [10-13]. Furthermore, hypothyroidism has been shown to cause edema in humans owing to increased capillary permeability to protein, which is reversed by thyroid hormone treatment [14]. These data suggest that hypothyroidism may reduce glomerular infiltration rate and promote urine protein loss.

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

Methods

We analyzed retrospectively 1364 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 MIU/L to 4.2 MIU/L, Free T4 12.0 pmol/L to 22.0 pmol/L. Participants were defined as having T2DM according to self-report, clinical reports, use of antidiabetic agents and HbA1c (≥ 6.5) [15]. HbA1c was expressed as percentage. High performance liquid chromatography was used. HTN was defined when the systolic blood pressure was ≥ 130 mmHg and/or diastolic blood pressure was ≥ 85 mmHg in addition to receiving any medication for hypertension [16]. Albuminuria was assessed by measurement of mean Albumin Excretion Rate (AER) on timed, overnight urine collections. We use a polyclonal radioimmunoassay for albumin measurement. Albuminuria was defined as AER ≥ 30 g/min in overnight urine collections (equivalent to 30 mg/g to 299 mg/g creatinine in a random spot sample) [17]. 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 eight groups: <20 years, 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 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.

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

Parameters		Total (1364)
Age (years)		55.9 ± 12.4
Gender	Male	379 (27.8)
	Female	985 (72.2)
Body mass index (kg/m^2)		31.8 ± 6.3
Hypertension		791 (58.0)
Albuminuria		515 (37.8)
Hypothyroidsm		423 (31.0)
HbA1c		8.1 ± 2.2
TSH (mIU/l)		4.4 ± 8.3
FT4 (pmol/l)		15.1 ± 2.9
Serum creatinine (µmol/L)		70.3 ± 26.1

Results

Out of the initial screening of 6023 subjects, 1364 subjects with T2DM were included. There were 861 (22.9%) male and 2899 (77.1%) were female with mean age 55.9 ± 12.4 and BMI 31.8 ± 6.3 kg/m^2, Table 1. There were 515 (37.8%), 791 (58.0%) and 423 (31.0%) with albuminuria, HTN and hypothyroidism respectively. The mean TSH and FT4 value was 4.4 ± 8.3 mIU/l and 15.1 ± 2.9 pmol/l respectively. Among cases of T2DM and albuminuria, there were 185 (35.9%) with hypothyroidism, Table 2. Regression analysis of odd ratio of risk factors for patients with type 2 diabetes and albuminuria with hypothyroidism showed that female gender, HTN, presence of hypothyroidism and HbA1c were associated with higher likely hood of albuminuria, (OR=1.8; 95% Confidence Interval [CI]=1.4, 2.4), p<0.0001), (OR=2.4; 95% CI=1.8, 3.1), p<0.0001), (OR=1.8; 95% CI=1.3, 2.3), p<0.0001) and (OR=1.2; 95% CI=1.1, 1.3), p<0.0001) respectively, Table 3. Cases with hypothyroidism were nonsignificantly showed no differences in HbA1c than cases with no hypothyroidism, 7.9 ± 2.3 vs. 8.1 ± 2.1 respectively, p=0.2. Hypothyroidsm with albuminuria was more prevalent in the seventh decade (32%), Figure 1. Hypothyroidsm was nonsignificantly more prevalent in females in the sixth decade and male in the seventh decade, Figure 2.

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

Parameters		Albuminuria		P value
		Present	Absent	
		515 (37.8)	849 (62.2)	
Age (years)		57.2 ± 12.5	55.1 ± 12.3	0.002
Gender	Male	171 (33.2)	208 (24.5)	0.001
	Female	344 (66.8)	641 (75.5)	
Body mass index (kg/m^2)		32.2 ± 6.5	31.6 ± 6.2	0.08
Hypertension		360 (69.9)	431 (50.8)	<0.0001
Hypothyroidism		185 (35.9)	238 (28.0)	0.003
HbA1c		8.7 ± 2.3	7.8 ± 2.1	<0.0001
TSH (mIU/l)		4.4 ± 7.6	4.4 ± 8.8	0.9
FT4 (pmol/l)		15.2 ± 2.9	15.0 ± 2.9	0.2
Serum creatinine (µmol/L)		76.2 ± 32.2	66.6 ± 20.7	<0.0001

Table 3: Regression analysis of odd ratio of risk factors for patients with type 2 diabetes and albuminuria with hypothyroidism.

Parameters	Odd Ratio	P value
Female gender	1.8 (1.4-2.4)	<0.0001
Age (years)	0.98 (0.88-1.1)	0.7
Body mass index (kg/m²)	1.02 (1.0-1.04)	0.05
Hypertension	2.4 (1.8-3.1)	<0.0001
Hypothyroidism	1.8 (1.3-2.3)	<0.0001
HbA1c	1.2 (1.1-1.3)	<0.0001

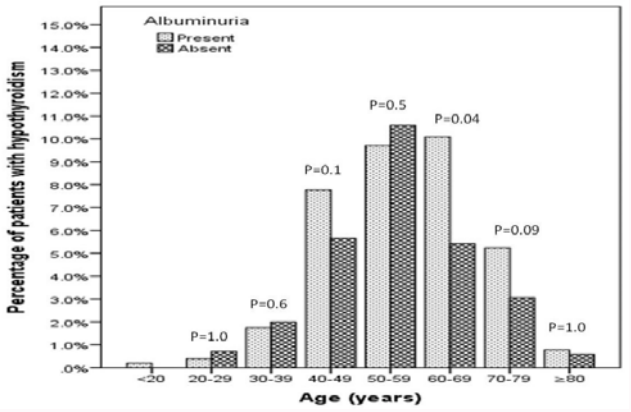

Figure 1: Age category groups and the frequency of hypothyroidism in patients with type 2 diabetes with and without albuminuria.

Discussion

The current study revealed that hypothyroidism in patients with T2DM complicated by albuminuria was found in 35.9%. The risk of albuminuria, defined as AER ≥ 30 g/min, increased by 1.8 for hypothyroidism as compared to euthyroidism, which remained significant after adjustment for other potential risk factors of albuminuria. To our knowledge, this is the first national and the largest study to explore the association between hypothyroidism and albuminuria in T2DM population. 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% to 20% of patients with chronic kidney disease not requiring renal replacement therapy, with the prevalence rising as the degree of renal impairment worsens [18,19]. The causal relationship between hypothyroidism and albuminuria is also uncertain. In patients with nephritic syndrome, the heavy urinary loss of thyroid hormone-binding proteins, including thyroxine binding globulin, thransthyretin, and albumin, results in a reduction in total T4 [20]. However, the thyroid gland is able to compensate the loss so that most patients remained in euthyroid state since serum free T4 or free T3 levels remain normal [20]. In a study involving 159 patients with nephrotic syndrome and 900 controls, nephrotic syndrome patients have slightly elevated TSH in normal range (1.81 vs. 1.34 mIU/L, P<0.001) and similar free T4 (13.1 vs. 13.1 pmol/L) levels as compared to controls [21]. In our analysis, the prevalence of

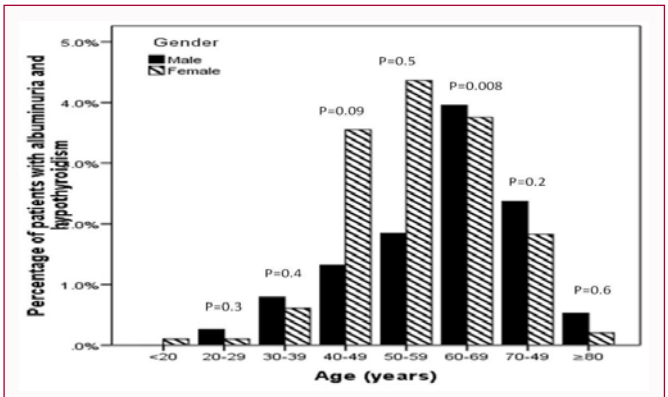

Figure 2: Age category groups and the frequency of hypothyroidism in patients with type 2 diabetes with and without albuminuria in correlation to gender.

clinical hypothyroidism was increased steadily from even no evident of albuminuria to albuminuria. The possibility of trace or mild albuminuria cause hypothyroidism seems unlikely.

In general, hypertension is well known risk factors for renal dysfunction among patients with T2DM [22]. In the multivariate analysis in the present study, hypertension was independently associated with albuminuria.

In general population, it was documented by many authors that hypothyroidism is more common in females [23-27]. In the present study, the prevalence of thyroid disorders was more in females as compared to males (77.3% versus 22.7%). This was not statistically significant, P=0.08. The non significant association could be explained by the small number of patients with hypothyroidism associated albuminuria. The prevalence of hypothyroidism is higher in women and is associated with an increased frequency of high titers of anti-thyroid antibodies which were not evaluated in our cohort [28].

Primary 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 [23-27]. We found the prevalence of hypothyroidism was found to be higher at the seventh decade and lower in patients with more age. The results of present study are in disconcordance with the previous study showed younger age decades (20 to 49 years) [29].

We aimed to identify the frequency of hypothyroidism in patients with T2DM complicated with albuminuria 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 albuminuria. In addition, the study shares the limitations of all retrospective studies [30].

We conclude that despite the limitations of this hospital-based retrospective study, hypothyroidism is highly prevalent in cohort of Saudis with albuminuria and T2DM. The majority of our patients with primary hypothyroidism in our finding were predominantly females. 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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References

1. LaFranchi S. Adolescent Thyroid Disorders. Adolesc Med. 1994;5(1):65-86.
2. Memon A, Berrington De González A, Luqmani Y, Suresh A. Family history of benign thyroid disease and cancer and risk of thyroid cancer. Eur J Cancer. 2004;40(5):754-60.
3. Okosieme OE, Marx H, Lazarus JH. Medical management of thyroid dysfunction in pregnancy and the postpartum. Expert Opin Pharmacother. 2008;9(13):2281-93.
4. Garmendia Madariaga A, Santos Palacios S, Guillén-Grima F, Galofré JC. The incidence and prevalence of thyroid dysfunction in Europe: a meta-analysis. J Clin Endocrinol Metab. 2014;99(3):923-31.
5. Faghilimnai S, Hashemipour M, Kelishadi B. Lipid profile of children with type 1 diabetes compared to controls: ARYA.J. 2006;2(1):36-8.
6. IDF Diabetes Atlas. 5th ed. 2012 update. International Diabetes Federation. 2012.
7. Lim VS, Fang VS, Katz AI, Refetoff S. Thyroid dysfunction in chronic renal failure. A study of the pituitary-thyroid axis and peripheral turnover kinetics of thyroxine and triiodothyronine. J Clin Invest. 1977;60(3):522-34.
8. Kaptein EM, Quion-Verde H, Chooljian CJ, Tang WW, Friedman PE, Rodriquez HJ, et al. The thyroid in end-stage renal disease. Medicine (Baltimore). 1988;67(3):187-97.
9. Hegedüs L, Andersen JR, Poulsen LR, Perrild H, Holm B, Gundtoft E, et al. Thyroid gland volume and serum concentrations of thyroid hormones in chronic renal failure. Nephron. 1985;40(2):171-4.
10. Lim VS. Thyroid function in patients with chronic renal failure. Am J Kidney Dis. 2001;38(4):S80-4.
11. Freeston J, Gough A. Reversible myopathy and renal impairment. J R Soc Med. 2004;97(3):124-5.
12. Makino Y, Fujii T, Kuroda S, Inenaga T, Kawano Y, Takishita S. Exacerbation of renal failure due to hypothyroidism in a patient with ischemic nephropathy. Nephron. 2000;84(3):267-9.
13. Mooraki A, Broumand B, Neekdoost F, Amirmokri P, Bastani B. Reversible acute renal failure associated with hypothyroidism: report of four cases with a brief review of literature. Nephrology (Carlton). 2003;8(2):57-60.
14. Connor A, Taylor JE. Renal impairment resulting from hypothyroidism. NDT Plus. 2008;1(6):440-1.
15. Wheatley T, Edwards OM. Mild hypothyroidism and oedema: evidence for increased capillary permeability to protein. Clin Endocrinol (Oxf). 1983;18(6):627-35.
16. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2019. Diabetes Care. 2019;42:S13-28.
17. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Himmelfarb CD, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018;71(6):1269-324.
18. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease. Part 5: Evaluation of laboratory measurements for clinical assessment of kidney disease. Am J Kidney Dis. 2002;39(2):S76-110.
19. Chonchol M, Lippi G, Salvagno G, Zoppini G, Muggeo M, Targher G. Prevalence of subclinical hypothyroidism in patients with chronic kidney disease. Clin J Am Soc Nephrol. 2008;3(5):1296-300.
20. Lo JC, Chertow GM, Go AS, Hsu CY. Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease. Kidney Int. 2005;67(3):1047-52.
21. Feinstein EI, Kaptein EM, Nicoloff JT, Massry SG. Thyroid function in patients with nephrotic syndrome and normal renal function. Am J Nephrol. 1982;2(2):70-6.
22. Gilles R, den Heijer M, Ross AH, Sweep FC, Hermus AR, Wetzels JF. Thyroid function in patients with proteinuria. Neth J Med. 2008;66(11):483-5.
23. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ. 1998;317(7160):703-13.
24. Dos Remedios Lv, Weber Pm, Feldman R, Schurr Da, Tsoi Tg. Detecting Unsuspected Thyroid Dysfunction By The Free Thyroxine Index. Arch Intern Med. 1980;140(8):1045-9.
25. Riniker M, Tièche M, Lupi GA, Grob P, Studer H, Bürgi H. Prevalence of various degrees of hypothyroidism among patients of a general medical department. Clin Endocrinol (Oxf). 1981;14(1):69-74.
26. Schectman JM, Kallenberg GA, Shumacher RJ, Hirsch RP. Yield of hypothyroidism in symptomatic primary care patients. Arch Intern Med. 1989;149(4):861-4.
27. Bastenie PA, Bonnyns M, Vanhaelst L. Natural history of primary myxedema. Am J Med. 1985;79(1):91-100.
28. Tunbridge WM, Brewis M, French JM, Appleton D, Bird T, Clark F, et al. Natural history of autoimmune thyroiditis. Br Med J (Clin Res Ed). 1981;282(6260):258-62.
29. Kaptein EM. Thyroid hormone metabolism and thyroid diseases in chronic renal failure. Endocr Rev. 1996;17(1):45-63.
30. Chang YC, Chang CH, Yeh YC, Chuang LM, Tu YK. Subclinical and overt hypothyroidism is associated with reduced glomerular filtration rate and proteinuria: a large cross-sectional population study. Scientific Reports. 2018;8:2031.