ORIGINAL ARTICLE

Co-Existence of Type 2 Diabetes Mellitus and Hypertension in Patients with Hypothyroidism

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ABTRACT

Aim: To evaluate the prevalence of co-existent type 2 diabetes mellitus and hypertension in patients with hypothyroidism.
Study design: Cross-sectional/observational study.
Place and duration of study: Endocrine Diabetes Clinic, Shaikh Zayed Hospital, Lahore from 1st October 2018 to 30th September 2019.
Methods: One hundred and fifty adult hypothyroid patients with more than 5 years history of hypothyroidism who visited endocrine Outpatient Department were enrolled. The prevalence of co-existent type 2 diabetes mellitus was assessed by 2 glycemic indicators [glycatedhaemoglobin (HbA1c), and fasting blood sugar level].The American Diabetes Association (ADA) criteria were used to define diabetes and the eight Joint National Committee (JNC 8) criteria was used to categorize the patients as hypertensive.
Results: One hundred and seven (71.33%) were females while 43 (28.66%) were males with mean age 53±12.45 years. Co-existent T2 diabetes mellitus and hypertension found in43 patients(28.66%) with mean systolic blood pressure was 158±14mmHg, fasting blood sugar level mean 184±36mg/dl and mean HbA1c was 10.28±2.5.
Conclusion: Keeping in view of high prevalence of co existent type 2 diabetes mellitus and hypertensionin patients with hypothyroidism (35%, more than 1/3rd) all patients on thyroxine>50 µg/day must be routinely screened for co-existent diabetes and hypertension even if no symptoms suggestive of hyperglycemia or hypertension exist.
Keywords: Co-existence, Hypothyroidism, Type 2 diabetes mellitus, Thyroxine>50 µg

INTRODUCTION

Hypothyroidism means low levels of thyroid hormones in body .The cause is either primary, when disease is lying in thyroid gland, secondary or tertiary cause are related to pituitary and hypothalamus respectively. The presentation of hypothyroidism may be either subclinical, overt, myxedema, end-organ effects and multisystem failure or with co-existent diabetes mellitus or hypertension[1,2.]

Thyroid disorders are 2-8 times higher in females than in males.7.5% of women and 2.8% of men were found to have high TSH in Colado prevalence study[3,4].

Type 2 diabetes mellitus (T2DM) and hypertension have an intersecting underlying pathology with hypothyroidism. Various studies have shown a high association of thyroid disorders (TDs) in patients with T2DM (12-23%) and hypertension (22.5%)[5,6].

Diabetes mellitus and hypothyroidism both are interdependent and co-exist. The possible reasons etiologies for co existence of diabetes mellitus and hypothyroidism are: genetic, biochemical or endocrinal.[7]

The possible pathogenesis of hypothyroid affecting the glucose hemostasis are multi-factorial (a) thyroid hormones directly control insulin secretion. In hypothyroidism, beta cells are less responsive to intra-gastric glucose leading to decreased insulin secretion, there is impaired lipid metabolism too[2]. (b) a direct relation between clinical and subclinical hypothyroidism and insulin resistance has been demonstrated in various pre-clinical studies[8-10].It was concluded that peripheral muscles became less responsive in hypothyroid states possibly due to errored degradation of leptin as a result of thyroid hormones deficiency[11]and (c) insulin resistance and β cell function are inversely correlated with level of serum thyroid stimulating hormone(TSH) i.e., the higher the TSH, the lower the β cell function. This concludes that low levels of thyroid hormones (high TSH i.e. hypothyroidism) leads to (i) weakened β cell function(decreased production and release of insulin) and also (ii) decreased effects of insulin on peripheral tissues.(insulin resistance).[12]Hypothyroidism is also linked to metabolic syndrome, adding more to the complex pathogenicity of insulin resistance[13].

Conversely, DM affects thyroid function in 3 probable ways; either (a) at the hypothalmus to control release of TSH from pituitary leading to tertiary or 2hypothyroidism (b) it also affects release of thyroid hormone from thyroid glands and (c) dysglycemia also effects conversion of T_4 to T_3 in the peripheral tissue[5].

If both hypothyroidism and diabetes mellitus co-exist, the microvascular complications (e.g. nephropathy, retinopathy) are more prevalent and more severe.[14] Subclinical hypothyroidism is more prevalent in diabetics, periodic evaluation of all diabetic patients for hypothyroidism should be done to avoid missing the co-existent disorder. In addition to T2 DM, co-existent HTN is also one of the associated clinical entity in patients with hypothyroidism. Hypothyroidism has been proved as secondary cause of HTN.[15]Patients with hypothyroidism have been reported to have greater radial wall thickness and compliance than euthyroid controls[16].

PATIENTS AND METHODS

This cross-sectional observational study was conducted at Endocrine & Diabetic clinic sheikh Zayed hospital Lahore from 1stOctober 2018 to 30thSeptember 2019. In hypothyroid patients who were on regular follow-up. All patients with iatrogenic (drug induced or surgical) hypothyroid, subclinical hypothyroidism (TSH < 20 or on no treatment for thyroid), type 1 diabetes mellitus, patients with organ dysfunction (kidney disease, ischemic heart disease or cardiomyopathy (CMP) were excluded. History of cerebrovascular disease (CVA) and peripheral arterial disease, who were already on intensive regimen for their diabetes were also excluded.After exclusion, hypothyroid patients who were on 50-250 µg of thyroxine/day were randomized, to assess for the co-existence of type 2 diabetes mellitus and hypertension.As hypothyroidism is more common in females,our randomized study included total of 107 females out of 150 patientswith ≥5 years of hypothyroidismwith age range of 35-65 years. In history we concentrated on life style, family history, h/o gestational diabetes, diabetic and hypertension status. The drug Hx included, dose of thyroxine, anti-hypertension drugs or any other alternative treatment. On physical examination, we recorded,weight (Kg),waist circumference at navel (cm) height, BMIs(kg/m^2), brachial BP, pulse pressure with electronic device. Minimum required investigations were done that include TSH, BUN, creatinine, fasting BSL, HbA1C. Diabetic status was assessed in all included population and patients were labelled diabetic if they fulfilled 2 of the criteria as per ADA Criteria. Blood pressure was checked in all included population at least twice at 2 different occasions and those fulfilling the criteria of HTN (defined in “study related definition”) were labelled as hypertensives. The data was entered and analyzed through SPSS-20.

RESULTS

Amongst the total 150 hypothyroid patients who were on >100 µg of thyroxine/day, 107 were females (71.33%) and 43 patients (28.66%) were males with mean age 53±12.45 years. Mean BMI was 37.6±4.37kg/m^2, mean systolic BP was 55±18 mmHg, mean waist was 86±17.47 cm, mean weight was 74±12.76 kg, mean fasting blood sugar level was 156±24 mg/dl and mean HbA1C was 8.4±2.45% (Table 1).The co-existent type 2 diabetes mellitus and hypertension found in43 patients (28.66%), diabetes alone found in 57 (38%) patients and 50 (33.33%) patients had pre-diabetes (Fig. 1).

Table 1: Demographic information of the patients

Variables	No.	%
Gender		
Male	43	28.66
Female	107	71.33
Age (years)	53±12.45	
BMI kg/m2	37.6+4.37	
Mean Waist cm	86±17.47	
Mean Weight kg	74±12.76	
Systolic BP mmHg	55±18	
Fasting BSL mg/dl	156±24	
HbA1C%	8.4±2.45	

Among 43 co-existent type 2diabetes mellitus and hypertension patients, 24 (55.81%) were females while 19 (44.19%) were males with mean age 52±11.71 years. Mean BMI was 38.6±4.19 kg/m2, mean waist (cm) was 85±13.73, mean weight (kg) 78±13.53 kg, mean systolic BP was 158±14 mmHg ranged between144-172 mmHg, fasting BSL mean 184±36mg/dl ranged between 148-220 mg/dl, and mean HbA1C was 10.28±2.5% ranged between 7.78-12.78% (Table 2).

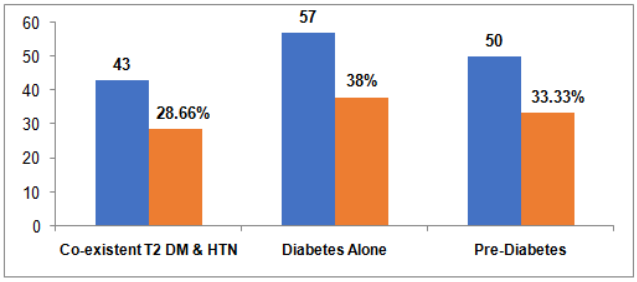

Fig. 1: Frequency of co-existent type 2 diabetes mellitus and hypertension among all the patients

Table 2: Characteristics of co-existent type 2 diabetes mellitus and hypertension patients

Variable	No.	%
Sex		
Male	19	44.19
Female	24	55.81
Age (years)	52±11.71	
BMI kg/m2	38.6±4.19	
Mean Waist cm	85±13.73	
Mean Weight kg	78±13.53	
Systolic BP mmHg	158±14	
Fasting BSL mg/dl	184±36	
HbA1C%	10.28±2.5	

DISCUSSION

Hypothyroidism means low levels of thyroid hormones in body. The cause is either primary, when disease is lying in thyroid gland, secondary or tertiary cause are related to pituitary and hypothalamus respectively. We randomly included the hypothyroid patients visiting to OPD over one year period. It included 71.33% females with age range of 35-65 years and 28.66% males with age ranging between 45-60 years, so hypothyroid females were 2.5 times more than their sex counterparts.Also it was found that females are more likely to suffer from hypothyroidism in their earlier age as compared to males These gender based differences in prevalence and age is matching with the ones quoted in the world literature[17,18].

In NHANES 1999-2002, the odds of having hypothyroidism were 5 times greater in persons aged 80 years and older than in individuals aged 12-49 years[17]. The Framingham study found hypothyroidism (TSH >10 mIU/L) in 5.9% of women and 2.4% of men older than 60 years[18].

This study clearly reported a high prevalence of co-existent T2DM (38%), and T2DM & HTN ((28.66%), pre-diabetes (33.33%), in hypothyroid patients. This prevalence of twin diseases in both genders is more as compared to documented prevalence in the existing international literature[1,19].

The prevalence studies published elsewhere have reported hypothyroidism prevalence to be 11%-23% in patients with T2DM.[20-22]Subramani et al[23] conducted a prevalence study in 2019 .The prevalence of diabetes was found to be 7.7% and 7.9-16.5% in the general population.[19]This varied observation in our study may be multi-factorial.To be mentioned here are long history of disease, poor knowledge of the illness, non specific clinical symptoms, poor compliance, lack of resources, alternate modes of treatment, unhealthy life style, social norms, resistant hypothyroidism, obesity, and late diagnosis.The prevalence of co-existent diabetes and hypertension in hypothyroidism, it was found that the hypothyroid pts who were more obese, had more BMIs were more likely to have co existent diabetes and hypertension.

In patients with co-existent type 2 diabetes mellitus and hypertension had more body mass index than the diabetes alone and pre-diabetes patients, this frequency of overweight and obese population is also concordant with that mentioned elsewhere in the literature, where the cause of this metabolic syndrome was also published.[24]

Kouidhiet al[24] published a study in 2013, they compared thyroid function in obese and/or diabetic patients with healthy normal controls, and concluded that TSH was directly associated with both overweight, obesity and insulin resistance.

Chakeret al[25] conducted a prospective study on Thyroid function and risk of type 2 diabetes in 2016. They concluded that the relative risk of pre-diabetes and diabetes is 1.09 times higher for every doubling of TSH level, and the higher FT4 level, the lower the risk of pre-diabetes and diabetes with each 1pmole/L increase in TSH the risk of developing diabetes in pre-diabetics is 0.93 times lower.[23]

This high prevalence of pre-diabetes in our study may be because we didn't relate the TSH values with the pre-diabetes/diabetes status in our study, had it done and it might matching results. On the other hand this contradictory finding in the prevalence of pre-diabetes in hypothyroid pts can be explained by other factors i.e. longer duration of the disease, severity of thyroid illness, poor compliance to thyroid treatment, history of gestational diabetes, or auto immune thyroid illness, sedentary life style, all of these are potential risk factors for the development of diabetes and pre-diabetes as mentioned in the international literature.[19,23]

CONCLUSION

The high prevalence of pre-diabetes, diabetes and hypertension associated with hypothyroidism. All of these patients were having hypothyroid for more than 5 years were either overweight or obese. This study further supports the routine and regular screening of obese, overweight patients for hypothyroidism, pre-diabetes, diabetes and hypertension as early diagnosis not only can lead to better management of hypothyroidism but can also be helpful to prevent and to decrease the complications associated with co-existing metabolic illnesses.

REFERENCES

1. Sunkari S, Godbole G, Ashok P, Kharche J, Joshi A. Association of hypothyroidism and type 2 diabetes in patients attending tertiary care hospital of Pune City. Natl J Physiol Pharm Pharmacol 2019;9(4):328-30
2. Kapadia KB, Bhatt PA, Shah J. Association between altered thyroid state and insulin resistance. J PharmacolPharmacotherap 2012;3: 156-60.
3. Blacher J, Kretz S, Sorbets E, Lelong H, Vallée A, Lopez-Sublet M. Epidemiology of hypertension: Differences between women and men. Press Med 2019;48(11 Pt 1):1240-43.
4. Choi HM, Kim HC, Kang DR. Sex differences in hypertension prevalence and control: Analysis of the 2010-2014 Korea National Health and Nutrition Examination Survey. PLoS One 2017; 12(5): e0178334.
5. Ahmed A. A study on prevalence of hypothyroidism in diabetics. Int J Med SciEduc 2014;1:120-4.
6. Mishra S, Mishra S, Behera BK. Thyroid dysfunction in patients with Type-2 diabetes mellitus in Eastern India. J Pharm Biomed Sci 2016;6:311-4.
7. Stanická S, Vondra K, Pelikánová T, Vlcek P, Hill M, Zamrazil V. Insulin sensitivity and counter-regulatory hormones in hypothyroidism and during thyroid hormone replacement therapy. ClinChem Lab Med 2005; 43(7): 715-20.
8. Dimitriadis G, Parry-Billings M, Bevan S, Leighton B, Krause U, Piva T, et al. The effects of insulin on transport and metabolism of glucose in skeletal muscle from hyperthyroid and hypothyroid rats. Eur J Clin Invest 1997; 27(6): 475-83.
9. Maratou E, Hadjidakis DJ, Peppaetal M. Studiesofinsulin resistance in patients with clinical and subclinical hyperthyroidism. Eur J Endocrinol 2010; 163(4): 625-30.
10. Owecki M, Nikisch E, Sowinski J. Hypothyroidism has no impact on insulin sensitivity assessed with HOMA-IR in totally thyroidectomized patients. ActaClinicaBelgica 2006; 61(2); 69-73.
11. Cettour-Rose P, Theander-Carrillo C, Asensio C, Klein M,Visser TJ,Burger AG, et al. Hypothyroidism in rats decreases peripheral glucose utilisation, a defect partially corrected by central leptin infusion. Diabetologia 2005; 48(4): 624-33.
12. Chen G, Wu J, Lin Y, Huang B, Yao J, Jiang Q, et al. Associations between cardiovascular risk, insulin resistance, beta-cell function and thyroid dysfunction: across-sectional study in She ethnic minority group of Fujian Province in China. Eur J Endocrinol 2010; 163(5): 775-82.
13. Ravishankar SN, Champakamalini, Venkatesh, Mohsin. A prospective study of thyroid dysfunction in patients with type 2 diabetes in general population. Arch Med 2013;5:2.
14. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, et al. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National health and nutrition examination survey (NHANES III). J ClinEndocrinolMetab 2002;87:489-99.
15. Ichiki T. Thyroid hormone and atherosclerosis. *VasculPharmacol 2010;* 52:151–6.
16. Giannattasio C, Rivolta MR, Failla M, Magnoni AA, Stella ML, Mancia G. Large and medium sized artery abnormalities in untreated and treated hypothyroidism. *Eur Heart J 1997;* 18: 1492–8.
17. Aoki Y, Belin RM, Clickner R, Jeffries R,Phillips L,Mahaffey KR. Serum TSH and total T4 in the United States population and their association with participant characteristics: National Health and Nutrition Examination Survey (NHANES *1999-2002).* Thyroid *2007; 17(12):1211-*23.\

18. Sawin CT, Castelli WP, Hershman JM, McNamara P, Bacharach P. The aging thyroid: thyroid deficiency in the Framingham Study. Arch Intern Med *1985;* 145(8):1386-8.
19. Demitrost L, Ranabir S. Thyroid dysfunction in type 2 diabetes mellitus: a retrospective study. Indian J EndocrMetab 2012;16(Suppl 2):S334-5
20. Han C, He X, Xia X,Li Y, Shi X, Shan Z, et al. Subclinical hypothyroidism and type 2 diabetes: a systematic review and meta-analysis. PLoS One 2015; 10(8): e0135233.
21. Kadiyala R, Peter R, Okosieme OE. Thyroid dysfunction in patients with diabetes: clinical implications and screening strategies. Int J ClinPract 2010;64(8):1130-39.
22. Turchi F, Ronconi V, di Tizio V, Boscaro M, Giacchetti G. Blood pressure, thyroid-stimulating hormone, and thyroid disease prevalence in primary aldosteronism and essential hypertension. Am J Hypertens 2011;24(12):1274-9.
23. Subramani SK, Yadav D, Mishra M, Pakkirisamy U, Mathiyalagen P, Prasad G. Prevalence of type 2 diabetes and prediabetes in the Gwalior-Chambal Region of Central India. Int J Environ Res Public Health 2019, 16(23): 4708.
24. Kouidhi S, Berhouma R, Ammar M, Rouissi K, Jarboui S, Clerget-Froidevaux MS, et al. Relationship of thyroid function with obesity and type 2 diabetes in euthyroid Tunisian subjects. Endocrine Res 2013; 38(1): 15-23