Thyroid dysfunction in Elderly people with type-2 Diabetes Mellitus

Rakesh Mudaraddi[1], Ramesh[2,*], Pramod S. Kamble[3]

[1]Associate Professor, [3]Tutor, SDM College of Medical Sciences & Hospital, Dharwad, Karnataka, [2]Assistant Professor, Dept. of Biochemistry, VIMS, Ballari, Karnataka

***Corresponding Author:**
Email: ramesh07ainoli@gmail.com

Abstract

Background: The prevalence of diabetes is rapidly increasing all over the world sparing no age group and some epidemiological studies indicated increase in the prevalence of thyroid disorders in elderly people. Worldwide studies have shown that there is increasing incidence of thyroid disorders among diabetic patients; this may complicate the metabolic regulation to a significantly dangerous level especially in older people. This reflects a strong interrelation between diabetes mellitus and thyroid dysfunction. The aim of our study is to know the association of thyroid disorders in elderly people with type-2 diabetes mellitus.

Materials and Methods: The study was carried out on 75 type-2 diabetic patients of more than 60 years with equal number of healthy controls. Blood glucose levels, Glycosylated hemoglobin (HbA1C), Thyroid hormones and Lipid profile were analyzed and results were compared with healthy individuals.

Results: In this study, the thyroid dysfunction was observed in 13.3% of case group. Out of 75 cases the frequency of hypothyroidism and hyperthyroidism were 9.33% and 3.97% respectively and euthyroid state contributed to 86.7%.

Conclusion: Thyroid disorders in elderly people with diabetes found to be significantly higher than non-diabetics. This helps in focussing not only treating diabetes alone, but also screening for thyroid disorders and managing both the clinical scenario, together will reduce morbidity and mortality rates.

Keywords: Elderly diabetic, Hyperthyroidism, Hyperglycemia, Subclinical Hypothyroidism, Diabetes Mellitus, Thyroid Dysfunction

Introduction

Diabetes Mellitus (DM) is a condition of impaired carbohydrate metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissue to insulin.(1)

The impact of diabetes on quality of life and on morbidity, mortality through the complications that affect the small and large vessels resulting in retinopathy, nephropathy, neuropathy, Ischaemic heart disease, large vessel obstruction has been emphasized by the findings of the national commission (USA) on diabetes and diabetes control and complication trial.(2)

Recently global estimates of diabetes prevalence clearly indicate an overall increase of diabetes in the developing countries.(3)

India has about 69 million individuals with DM in 2015. Worldwide more than 415 million adults have diabetes and this number is estimated to increase to 642 million by 2040.(4)

Next to diabetes, the prevalence of thyroid disease appears to be high among endocrine disorders in general population. Studies indicated that there could be co-existence of the both the diseases.(5,6)

Thyroid disease is a pathological state that adversely affects diabetic control and commonly found in most forms of DM, which is associated with advanced age in type-2 diabetes and autoimmune diseases in type-1diabetes.(6)

DM appears to influence thyroid function in two sites; firstly at the level of hypothalamic control of TSH release and secondly at peripheral tissue by converting T4 to T3. Hyperglycemia causes reduction in hepatic concentration of T4-5 deiodinase, low serum concentration of T3, raised levels of reverse T3 and low, normal or high levels of T4. Thyroid hormone regulate metabolism and diabetes can alter metabolism.(8)

The purpose of current study is to bring attention towards improving care of elderly people with diabetes in association with thyroid diseases by routinely screening these profiles together at regular intervals.

Materials and Methods

Number of subjects visiting to clinical OPD and those admitted in wards with more than 60 years of age were included in this study. Study was conducted on total 150 subjects consisting equal number of cases and healthy controls. The study protocol was approved by institutional ethical committee. Selection of cases and controls were made on the basis of blood glucose levels and Glycosylated hemoglobin (HbA1C) levels.

Individuals with type 2 DM irrespective of glucose control and receiving treatments such as insulin, oral hypoglycaemic drugs without any complications were included. Exclusion criteria is patients with type 1 diabetes, already proven thyroid disorders and on treatment, liver diseases, renal diseases, cardiac diseases, exposure to radiation and surgeries like thyroidectomy, consumption of alcohol and drugs like steroids, lithium etc.

Venous blood sample was used for this study after obtaining informed consent from the patient. Serum

collected after centrifugation used for estimating Free T_3 (FT_3), Free T_4 (FT_4) and Thyroid Stimulating Hormone (TSH) by chemilumenescence immunoassay (CLIA) methods on fully automated hormone analyzer (Siemens Advia centaur cp).

Analysis of biochemical parameters were done on fully automated chemistry analyzer (Siemens dimension RXL Max) which included serum fasting and postprandial blood sugar (FBS and PPBS) by Hexokinase method, Total Cholesterol by Cholesterol-Oxidase method, High Density Lipoprotein (HDL) by direct HDL-C method, Low Density Lipoprotein (LDL) by direct LDL-C method, Triglycerides (TG) by enzymatic method. Whole blood used for assessing Glycosylated Hemoglobin (HbA_{1C}) by High Performance Liquid Chromatography (HPLC) method (Bio-Rad D10).

Statistical analysis was done by using student 't' test using SPSS version 20.0(trial version).

Results

Table 1: Comparison of Biochemical parameters in control and cases

Parameters	Controls Mean ± SD (n=75)	Cases Mean ± SD (n=75)	p value
FBS (mg/dl)	89.86 ± 9.11	137.82 ± 48.01	<0.0001
PPBS (mg/dl)	102.26 ± 18.58	201.6 ± 73.07	<0.0001
Hb A1c (%)	5.30 ± 0.39	7.65 ± 1.22	<0.0001

Table 2: Demographic representation of control and cases

Demographic criteria	Thyroid status		Sex	
			Male	Female
Controls (n=75)	Euthyroid	71	43	28
	Thyroid disorder	4	1	3
Diabetic (n=75)	Diabetis with Euthyroid	65	36	29
	Diabetis with thyroid disorder	10	3	7

Table 3: Lipid profile in Diabetics with Thyroid Disease

Parameters	Hypothyroidism Mean ± SD	Subclinical Hypothyroidism Mean ± SD	Subclinical Hyperthyroidism Mean ± SD
Total cholesterol	270.67 ± 13.65	193.30 ± 51.08	136.67 ± 4.72
HDL-C	36.33 ± 9.02	43.40 ± 3.80	46.0 ± 10.81
LDL-C	185.00 ± 10.44	122.40 ± 43.80	71.33 ± 6.35
Triglycerides	200.67 ± 83.77	147.5 ± 59.57	95.67 ± 42.83

In the present study we analyzed blood glucose (fasting and post prandial), Glycosylated hemoglobin (HbA**1C**), thyroid profile (FT3, FT4 and TSH) and lipid profiles in all subjects.

Table 1 represents level of biochemical parameters like fasting, postprandial blood sugar and Glycosylated hemoglobin, which helped in separating cases and controls. The prevalence of FBS, PPBS and HbA**1C** levels were significantly (P< 0.0001) elevated in case group than control group.

Distribution of thyroid disease among cases and controls were shown in table no. 2. Control group has 4 (5.33%) thyroid disorder subjects and remaining 71 (94.67%) individuals with euthyroid state. Among diabetic group 10 (13.33%) persons had thyroid disorder of which 7 (9.33%) were females and 3 (4%) were males. Case group comprised total 39 males (52%) and 36 females (48%) while control group consisting 44 males (58.67%) and 31 females (41.33%).

Mean and SD for lipid parameters among thyroid disorders of diabetic group presented in Table 3. Overt hypothyroid and subclinical hypothyroid groups showed elevated levels of total cholesterol, LDL cholesterol and triglycerides. But, hyperthyroidism was not associated with gross lipid alterations.

Discussion

Type-2 DM results from insulin resistance, which may be combined with relatively reduced insulin secretion and is due primarily to life style factors and genetics.[9]

Defective insulin secretion leads to various metabolic aberrations in type-2 DM, spanning from hyperglycemia due to defective insulin stimulated glucose uptake and up regulated hepatic glucose production, along with dyslipidemia, which includes impaired homeostasis of fatty acids, triglycerides and lipoproteins.[10]

Thyroid disease is a pathological state that adversely affects diabetic control and is commonly found in most forms of DM which is associated with advanced age in type-2 diabetes and autoimmune diseases in type-1 diabetes.[8]

In the present study we have evaluated thyroid profile in type-2 diabetics and compared it with healthy non diabetic individuals of more than 60 years of age. Out of 75 type-2 diabetics, 86.7% falls into euthyroid state and remaining 13.3% had thyroid abnormalities. While control group has only 5.33% of thyroid abnormalities and remaining 94.67% without abnormalities.

It was observed that there was an increased frequency of thyroid dysfunction with advancing age and higher prevalence of thyroid disease in women compared to men and in diabetic subjects compared to non diabetic. Several reports documented a higher than normal prevalence of thyroid dysfunction in diabetic population.[11]

Impaired thyroid function can be assessed clinically based on symptomatic presentations and

laboratory findings. Thyroid dysfunction involves either inadequate thyroid hormone secretion resulting in hypothyroidism or if excessively produced leading to hyperthyroidism.

Very less attention is given to diagnosis of thyroid diseases in diabetics as they are diagnosed in only about half of the patients. Hypothyroidism and DM show clinical signs and symptoms like fatigue, lethargy and weight gain.[12]

In our study, proportion of subclinical hypothyroidism (6.66%) is the leading contributor among thyroid disorders, involving more number of females than males. Study of Catia Cristina Silva Sousa Vergara Palma et al, showed that frequency of subclinical hypothyroidism was 12% with the age of 60.7 ± 10.6 years.[13]

The proportion of overt hypothyroidism was 2.67% in this study which is distributed equally between two genders. 12% of overt hypothyroid cases were observed in the study of R. Anilkumar et al with mean age of 55 years.[14] Compare to our study, these studies have shown higher frequency of hypothyroidism in diabetics than healthy controls.

In hypothyroidism there is reduction in the rate of glucose absorption, gluconeogenesis and glucose production (and utilization) and glycogen synthesis (and degradation) leading to increased glycogen level.[15]

Glucose disposal is decreased in hypothyroidism, while glucose stimulated insulin secretion is increased, presumably because of insulin resistance. Insulin resistance, present in both overt hypothyroidism and subclinical hypothyroidism, may increase cardiovascular risk, especially when it is related with other frequently associated risk factors such as hyperlipidaemia and elevated blood pressure.[16,17,18]

Only a case of overt hyperthyroidism (1.3%) is observed in this study and one each in male and female presented with subclinical hyperthyroidism (2.67%).

Hyperthyroidism has been associated with insulin resistance which has been linked with elevated glucose turnover, increased intestinal glucose absorption, elevated hepatic glucose output, increased free fatty acid concentrations, increased fasting and or postprandial insulin an pro-insulin levels, and increased peripheral glucose transport accompanied by glucose utilization.[19,20]

Among lipid profiles triglycerides, LDL cholesterol and total cholesterol levels were elevated in hypothyroidism especially in overt hypothyroidism. But, hyperthyroidism was not associated with gross lipid alterations.

Insulin resistance is a condition which occurs in both hypothyroidism and hyperthyroidism.[19] Insulin resistance also leads to impaired lipid metabolism according to recent findings.[21]

Rate of local lipolysis in the abdominal subcutaneous adipose tissue was a result of modulation of norepinephrine (NE) levels and adrenergic post receptor signalling by thyroid hormones.[22] According to Mory G et al, thyroid hormones are necessary for the mobilization of the tissue lipids especially brown adipose tissues (BATs) which are the fuel for the production of heat.[23]

The clinical presentation of patients with thyroid dysfunction varies widely. If patients present with subtle or atypical symptoms, a delay in the diagnosis and treatment can potentially worsen the outcome.[24]

The situation is further complicated given with non specific symptoms and signs of thyroid dysfunction are often attributed to ageing or co-existing illness.[25]

Many more studies are needed to know the prevalence of thyroid dysfunction in elderly people with type 2 diabetes mellitus and special attention should be paid towards understanding mechanism of these endocrine disorders at genetic levels especially in geriatric age group.

Overlapping of two common endocrine disorders such as diabetes and thyroid dysfunction in elderly people challenges the management plan especially if individuals presents with vague and non-specific symptoms.

Conclusion

In our study, we found 13.3% thyroid disorders in elderly type 2 diabetics as compared to 5.3% in healthy group.

Ageing itself results in altered health status and when it is accompanied with diabetes and thyroid diseases will further hamper health of an individual. Elderly people presenting with non-specific clinical manifestations needs special consideration, as diabetes and thyroid dysfunction worsens metabolic control and impairs the treatment aspect. Therefore, optimal management of diagnosed type-2 diabetes patients also needs frequent testing of thyroid profile either annually or if possible biannually. Management of these two conditions together may improve quality of life, helps in effective treatment and reduce complications of diabetes mellitus.

References

1. Editorial; Epidemic of diabetes in urban Nepal - Time to act. Journal of Nepal Medical Association, 2003;42:1-11.
2. Satish R, Mohan V. Diabetes and Thyroid diseases. Rev Int J Diabetes Dev Countries. 2003;23:120-123.
3. Sayeed MA, Rumi MA, Banu A, Hussain LA, Khan A, K Azad. Effect of socioeconomic risk factors on the difference in prevalence of diabetes between rural and urban populations in Bangladesh. Diabetes Care, 1997;20(4):551-555.
4. Ranjit Unnikrishnan, Ranjit Mohan Anjana, Vishwanathan Mohan. Nature Reviews/ Endocrinology. Vol;12. June 2016;357-370.
5. Perros P, Mc Crimmon RJ, Shaw G and Frier BM. Frequency of thyroid dysfunction in diabetic patients: value of annual screening. Diabet Med. 1995;12(7):622-627.

6. Smithson MJ. Screening for thyroid dysfunction in a community population of diabetic patients. Diabet Med. 1998;15(2):148-150.
7. Mouradian M, Abourizk N. Diabetes mellitus and thyroid disease. Diabetes Care. 1983;6:512-520.
8. Shah SN. Thyroid disease in diabetes mellitus. J Assoc Physicians India. 2007;32(12):1057-1059.
9. Riserus U, Willett WC, Hu FB. Dietary fats and prevention of type-2 diabetes. Prog Lipid Res. 2009;48(1):44-51.
10. JD Baxter and P Webb. Thyroid hormone mimetics: potential applications in atherosclerosis, obesity and type 2 diabetes. Nature Reviews Drug Discovery. 2009;8(4):308-320.
11. Perros P, McCrimmon RJ, Shaw G, Frier BM. Frequency of thyroid dysfunction in diabetic patients: value of annual screening. Diabet Med. 1995;12:622-627.
12. Ghazali SM and Abbiyesuku FM. Thyroid dysfunction in type 2 diabetics seen at the university college hospital, Ibadan, Nigeria. Nig J Physiol Sci. 2010;25(12):173-179.
13. Catia Cristina Silva Sousa Vergara Palma et al. Prevalence of thyroid dysfunction in patients with diabetes mellitus. Diabetology and Metabolic syndrome. 2013;5(58):1-5.
14. R Anilkumar, KR Narasimhasetty, R Lalita, SB Shetty. Prevalence of thyroid dysfunction among type 2 diabetes subjects in south India. International Journal of Clinical Cases and Investigations. 2013;5(6):93-100.
15. Mohn A, Di Michele S, Di Luzio R, Tumini S and Chiarelli F. The effect of subclinical hypothyroidism on metabolic control in children and adolescents with type 1 diabetes mellitus. Diab Med. 2002;19:70-73.
16. Maratou E, Hadjidakis DJ, Kollinas A et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. European Journal of Endocrinology. 2009;160:785-790.
17. Brenta G, Celi FS, Pisarev M et al. Acute thyroid hormone withdrawal in athyreotic patients results in state of insulin resistance. Thyroid. 2009;19:665-669.
18. Rotondi N, Den Elzen WP, Bauer DC et al. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. JAMA. 2010;304:1365-1374.
19. Brenta G, Celi FS, Pisarev M et al. Acute thyroid withdrawal in athyreotic patients results in a state of insulin resistance. Thyroid. 2009;19(6):665-669.
20. GD Dimitriadis and SA Raptis. Thyroid hormone excess and glucose intolerance. Experimental and Clinical Endocrinology and Diabetes. 2001;109(2):225-239.
21. KB Kapadia, PA Bhatt and JS Shah. Association between altered thyroid state and insulin resistance. Journal of Pharmacology and Pharmacotherapeutics. 2012;3:156-160.
22. M Haluzik, J Nedvidkova, V Bartak et al. Effects of hypo and hyperthyroidism on non adrenergic activity and glycerol concentrations in human subcutaneous abdominal adipose tissue assessed with microdialysis. Journal of Clinical Endocrinology and Metabolism. 2003;88(12):5605-5608.
23. G Mory, D Ricquier, P Pesquies, P Hemon. Effects of hypothyroidism on the brown adipose tissue of adult rats: comparison with the effects of adaptation to cold. Journal of Endocrinology. 1981;91(3):515-524.
24. Trivalle C et al. Differences in the signs and symptoms of hyperthyroidismin older and younger patients. J Am Geriatr Soc. 1996;44:50-53.
25. Mooradian AD. Asymptomatic hyperthyroidism in older adults: is it a distinct clinical and laboratory entity? Drugs Aging. 2008;25:371-380.