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Comparison of Thyroid Functional Status among Different Levels of Glycaemic Status

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Abstract **Original Research Article**

Background: Diabetes mellitus (DM) is a leading cause of death and disability worldwide. Its global prevalence was about 8% in 2011 and is predicted to rise to 10% by 2030. Nearly 80% of people with diabetes live in low- and middle-income countries. Asia and the eastern Pacific region are particularly affected. In Bangladesh, which had a population of 149.8 million in 2011, a recent meta-analysis showed that the prevalence of diabetes among adults had increased substantially, from 4% in 1995 to 2000 and 5% in 2001 to 2005 to 9% in 2006 to 2010. According to the International Diabetes Federation (IDF), the prevalence will be 13% by 2030. ***Methods:*** This cross-sectional study was carried out on newly detected type-2 DM patients [n=200, m/f: 81/119; age: 41.1±8.3; BMI (kg/m^2): 26.0±4.2; mean±SD] recruited consecutively from the department of Endocrinology, BSMMU. History and relevant clinical examination were recorded. Free thyroxine (FT4), thyroid stimulating hormone (TSH), anti-TPO and anti-TG antibody were tested Chemiluminescence Immunoassay System (Germany). ***Results:*** Highest frequency for positive anti-thyroid antibody (87.5%) was observed in group having TSH ≥10 m IU/L followed by 66.7% in the group having TSH (5-10) m IU/L, while only 2.8% in the group having TSH <5 m IU/L (p<0.001). There was no significant difference either for level of FT4 (14.0±4.5 vs 14.1±2.2 vs 13.9±1.5; p= 0.925) or for TSH (3.4±5.0 vs 3.7±9.7 vs 2.3±1.6; p= 0.691) or for the antibody status (p= 0.721) among different levels of HbA1c. No significant correlations of FPG, 2Hr75gPPG and HbA1c was found with any of FT4, TSH, anti-TPO and anti-TG antibodies (p= NS for all). Logistic regression revealed anti-TPO antibody as independent predictor for thyroid dysfunction in subjects with diabetes mellitus (p<0.001). ***Conclusion:*** A comparative study of thyroid hormone levels in diabetic and non-diabetic patients revealed that patients with type-2 DM had significantly lower serum FT3 levels (p<0.001) compared to the control groups. There were no significant differences observed in serum FT4 (p= 0.339) and TSH (p= 0.216) levels between the control and study subjects.

Keywords: Hypothyroidism, diabetes mellitus, thyroid dysfunction.

INTRODUCTION

Hypothyroidism is by far the most common thyroid disorder and is more common in older women. Approximately 4 million people in the United States are hypothyroid and receive thyroxine replacement therapy. By contrast, hyperthyroidism is much less common, with a female-to-male ratio of 9:1. Graves' disease is common among young adults while toxic multi-nodular goiters tend to affect the older age-groups [1].

Thyroid hormones are functionally antagonistic to insulin. Both insulin and thyroid hormones are involved in cellular metabolism and excess and deficit of either one can result in functional derangement of the other [2]. Insulin resistance and β-cell function are inversely correlated with TSH, which may be explained by the insulin- antagonistic effects of thyroid hormones along with an increase in TSH [3]. The high serum TSH corresponds to lower triiodothyronine (T3) and thyroxine (T4) levels which weakens the insulin antagonistic effects. This observation demonstrates that insulin imbalance is associated closely with thyroid dysfunction and is mediated via beta-cell dysfunction [2]. Diabetes

mellitus appears to influence thyroid function in two sites; firstly at the level of hypothalamic control of TSH release and secondly at the conversion of T4 to T3 in the peripheral tissue [4]. In hypothyroidism, the synthesis and release of insulin is decreased. The rate of hepatic glucose output is decreased probably due to reduced gluconeogenesis. Long term thyrotoxicosis has been shown to cause beta cell dysfunction resulting in reduced pancreatic insulin content, poor insulin response to glucose and decreased rate of insulin secretion [5]. A recent study involving subjects from a Chinese population found a higher TSH level in patients with metabolic syndrome compared to that in the nonmetabolic syndrome group suggesting that subclinical hypothyroidism may be a risk factor for metabolic syndrome. Furthermore, an increased risk of nephropathy was shown in patients with type 2 DM with subclinical hypothyroidism which could be explained by the decrease in cardiac output and increase in peripheral vascular resistance seen with hypothyroidism and the resulting decrease in renal blood flow and glomerular filtration rate. In 2005, Den Hollander *et al.*, reported that treating hypothyroidism improved renal function in patients with diabetes mellitus [6]. As for retinopathy, Yang *et al.*, demonstrated recently that patients with DM with subclinical hypothyroidism have more severe retinopathy than euthyroid patients with DM [6].

In Bangladesh, a comparative study of thyroid hormone levels in diabetic and non-diabetic patients revealed that patients with type-2 DM had significantly lower serum FT3 levels compared to the control groups but there were no significant differences observed in serum FT4 and TSH levels between the control and study subjects [7]. But no data are available regarding frequency of thyroid dysfunction among patients with diabetes mellitus in our country. Present study is undertaken to know the frequency of thyroid dysfunction in newly detected patients with type-2 diabetes mellitus.

OBJECTIVES

General Objective

- To compare thyroid functional status among different levels of glycaemic status.

Specific Objective

- To see the frequency of thyroid dysfunction (Primary hypothyroidism, Subclinical hypothyroidism, Thyrotoxicosis, Subclinical thyrotoxicosis) and thyroid autoimmunity among adult patients with newly detected type-2 DM.
- To observe the correlation between glycaemic profile and thyroid functional status.
- To see the predictors of thyroid dysfunction in adult patients with newly detected type-2 DM.

METHODOLOGY

Type of study	**Cross-sectional observational study**
Place of study	Department of Endocrinology, BSMMU
Study period	January 2017 to January 2018
Study population	Adult (≥18 year) patients with newly detected type-2 DM
Sampling technique	Samples were collected consecutively by purposive sampling technique
Sample Size	The sample size of the study were 200

Inclusion Criteria

- Adult (age ≥18 yrs) patients with newly detected type-2 DM irrespective of sex.

Exclusion Criteria

- Patient with thyroid disorder on treatment.
- Patients with acute illness (sepsis, acute MI, severe heart failure, recent admission in intensive care unit). Patients with established hepatic dysfunction.
- Patients with acute or chronic renal failure
- Patients with drug induced hyperglycemia (high dose steroids, pentamidine, diazoxide).
- GDM and other specific types of diabetes.
- Unwilling patient to participate in the study.

Study Procedure

A data collection sheet containing general information on demographic characteristics, family history of thyroid disease, diabetes mellitus, history of smoking, presence of any co morbidities like hypertension, ischemic heart disease, dyslipidaemia etc. were filled up for each patient on the first day. Clinical evaluation was also done including estimation of height (cm), weight (kg), BMI (kg/m^2) and BP (mmHg), waist circumference (cm). Then 5 ml of venous blood was drawn from each eligible subject. Serum was separated and transported to the National Institute of Nuclear Medicine & Allied Sciences (NINMAS), BSMMU. Assay of serum FT4, TSH, anti-TPO and anti-TG antibody of collected samples were done at NINMAS lab, BSMMU without causing any harm to quality using SIEMENS ADVIA Centaur XPT Chemiluminescence Immunoassay System (Germany). Reports were collected and preserved in raw data sheet.

Data Processing and Analysis

Data from the study were analyzed using computer based SPSS Program (version 23.0).

For Data Collection

Data collection sheet

For Collection of Sample

Vaccoutainer tubes, eppendorfs, syringes and necessary materials

Statistical Analysis

Data were analyzed using computer based SPSS program (version 23.0). All collected data were checked and cleaned cautiously. Data were described in frequencies or percentages for qualitative values and mean (±SD) for quantitative values. Subgroups made on the basis of clinical and biochemical findings were compared by student t -test or chi-square test as applicable. Pearson correlation was be used to see correlation between different variables. Logistic regression was done to detect different predictors of thyroid dysfunction. P values less than or equal to 0.05 was considered as significant.

RESULT

Table 1: Comparison of anti-thyroid antibody status with thyroid function among study population (n=200)

Thyroid functional status	Positive N (%)				Negative N (%)	P value
	Both	Only TPO-Ab	Only TG-Ab	Total		
Euthyroid	1 (0.6)	4 (2.3)	0	5 (2.9)	169 (97.1)	**<0.001**
Hypothyroidism	5 (83.3)	0	0	5 (83.3)	1 (16.7)	
Subclinical hypothyroidism	2 (11.8)	10 (58.8)	0	12 (70.6)	5 (29.4)	
Hyperthyroidism	0	0	0	0	1 (100)	
Subclinical Thyrotoxicosis	0	0	0	0	2 (100)	

Within parenthesis are percentages over row total.Analysis done by Fisher's Exact test. *Anti-thyroid antibod**y=** Anti-thyroid peroxidase antibody (anti-TPO Ab), Anti-thyroglobulin antibody (anti-TG Ab)

Table 2: Comparison between anti-thyroid antibody status with different levels of TSH among study population (n=200)

TSH (m IU/L)	*Anti-thyroid antibody		Total N (%)	P value
	Positive N (%)	Negative N (%)		
<5	5 (2.8)	172 (97.2)	177 (100)	**<0.001**
(5-10)	10 (66.7)	5 (33.3)	15 (100)	
>10	7 (87.5)	1 (12.5)	8 (100)	

Within parenthesis are percentages over row total. Analysis done by Fisher's Exact test; *Anti-thyroid antibod**y=** Anti-thyroid peroxidase antibody (anti-TPO Ab), Anti-thyroglobulin antibody (anti-TG Ab), TSH= Thyroid stimulating hormone

Table 2 describes the comparison of FT4 and TSH among different levels of HbA1c and there was no significant difference either for level of FT4 (14.0±4.5 vs 14.1±2.2 vs 13.9±1.5; p= 0.925) or for TSH (3.4±5.0 vs 3.7±9.7 vs 2.3±1.6; p= 0.691) among different levels of HbA1c (<7% vs 7-9.9% vs ≥10%).

As shown in table 3 frequency of positive and negative anti-thyroid antibodies were not statistically different among different levels of HbA1c (p= 0.721).

Table 3: Comparison of FT4 and TSH among different levels of HbA1c among study population (n=200)

Thyroid function test	HbA1c %			P value
	<7	(7-9.9)	≥10	
FT4 (pmol/L) mean±SD	14.0±4.5	14.1±2.2	13.9±1.5	0.925
TSH (mIU/L) mean±SD	3.4±5.0	3.7±9.7	2.3±1.6	0.691

Analysis done by oneway ANOVA. FT4 = Free thyroxine, TSH = Thyroid stimulating hormone, HbA1c = Hemoglobin A1c

Table 4: Comparison of anti-thyroid antibody status with different levels of HbA1c among study population (n=200)

Antibody status	HbA1c (%)			Total	P value
	<7	(7-9.9)	≥10		
Positive	4 (18.2)	16 (72.7)	2 (9.1)	22 (100)	0.721
Negative	38 (21.3)	111 (62.4)	29 (16.3)	178 (100)	

Within parenthesis are percentages over row total. Analysis done by Fisher's Exact test, HbA1c = Hemoglobin A1c

Clinical Characteristics; Relation with Thyroid Function, Biochemical Parameters

Comparison of clinical parameters of the study population among different thyroid functional status in table 5 shows that there was significant difference of mean BMI among various subgroups of thyroid functional status (p= 0.014). Turkey's post hoc analysis shows mean BMI of patient with subclinical hypothyroidism was significantly higher than that of euthyroid subjects (28.7±4.7 vs 25.8±4.0, p= 0.030).

As shown in table 6, comparison of glycaemic parameters of the study population among different thyroid functional status shows that there was no significant difference of glycaemic parameters among different thyroid functional status.

Table 5: Comparison of clinical characteristics of the study population among different thyroid functional status (n=200)

Variables	Euthyroid	Hypothyroidism	Subclinical hypothyroidism	*Thyrotoixcosis	P value
	mean±SD				
BMI (Kg/m^2)	25.8±4.0	27.1±6.8	28.7±4.7	22.0±3.9	**0.014**
WC (cm)	96.9±9.4	96.5±6.5	102.3±7.0	89.0±1.0	0.052
SBP (mmHg)	132.9±12.9	136.7±15.0	127.6±14.4	126.7±15.3	0.305
DBP (mmHg)	75.3±7.9	75.0±10.5	75.9±8.7	66.7±5.8	0.328

By one way ANOVA *Thyrotoxicosis=Hyperthyroidism and Subclinical thyrotoxicosis only for this table. BMI=Body mass index, WC=Waist circumference, SBP=Systolic blood pressure, DBP=Diastolic blood pressure.

Turkey's post hoc analysis shows mean BMI of patient with subclinical hypothyroidism was significantly higher than that of euthyroid subjects (28.7±4.7 vs 25.8±4.0, p = 0.030).

Table 6: Comparison of glycemic parameters of the study population among different thyroid functional status (n=200)

Variables	Euthyroid	Hypothyroidism	Subclinical hypothyroidism	*Thyrotoixcosis	P value
	mean±SD				
FPG (mmol/L)	9.3±1.9	8.9±1.9	9.1±1.8	9.2±1.9	0.933
2Hr PPG (mmol/L)	16.6±3.3	15.8±2.7	16.9±3.9	16.0±3.9	0.895
HbA1c (%)	8.3±1.5	7.9±1.4	8.4±1.6	8.2±1.4	0.938

By one way ANOVA *Thyrotoxicosis=Hyperthyroidism and Subclinical thyrotoxicosis only for this table. FPG = Fasting plasma glucose, 2HrPPG = Plasma glucose 2hour after 75gram glucose load, HbA1c = Hemoglobin A1c

DISCUSSION

In a study in India by S Mukherjee (2015), it was revealed that 22 subjects with diabetes mellitus out of 79 with thyroid dysfunction were positive for anti-TPO antibodies (27.84% of total thyroid abnormality) which are much higher than the frequency detected in present study [8]. On the other hand, 7 subjects without any thyroid dysfunction showed anti-TPO antibody positivity (17.07%) as observed by them which were 2.9% found by us. Therefore, presence of thyroid dysfunction and positivity of anti-thyroid antibody is neither obligatory association nor mutually exclusive with diabetes that could better be accomplished by thinking for need of testing for hormonal abnormality and anti-thyroid antibody status in subjects with newly detected DM. Owing to scanty number of investigations on thyroid autoimmunity in diabetic subjects it is not possible to assess clearly over the relative status of present findings in context to previously prevailing thyroid functional status in diabetic population. There were few studies on thyroid autoimmunity in this country; but most of them were in general population. Therefore, assessing over status of thyroid dysfunction in diabetic population will need investigation in mass scale [9].

In a study done by Khurana *et al.*, (2015), out of 32 subjects with diabetes mellitus who had thyroid dysfunction, 21.9% has family history of thyroid disorder [10]. Present study also found the prevalence of thyroid disorder in patients who had no family history of thyroid disorder. These findings are indicative of different impact of family history of thyroid disorder and diabetes over newly detected thyroid dysfunction in any subject. Khurana *et al.*, (2015) also observed that out of 32 patients with diabetes mellitus who had thyroid dysfunction, 6 (18.75%) had HbA1C<7 and 26 (81.25%) had HbA1C ≥7 [10]. The prevalence of thyroid dysfunction was found to be more in patients with HbA1C ≥7 as compared to patients with HbA1C< 7. This difference was highly significant statistically. But in the present study, the comparison of FT4 and TSH among different levels of HbA1c did not show any significant difference either for level of FT4 or for TSH

among different levels of HbA1c. This disparity may be attributable to limited number of subjects in their study. Unless observed in mass scale, no definite inference can be plotted on the matter.

Comparing the clinical parameters of the study population among different thyroid functional status, there was significant difference of mean BMI among various subgroups of thyroid functional status. This findings were similar to a study done by Khurana *et al.*, 2015, whereupon out of 32 diabetic patients who had thyroid disorders, 7 (21.87%) had BMI < 25, 6 (18.75%) had BMI between 25 - 30 and 19 (59.37%) had BMI > 30 [10]. Though apparently it seems that BMI is related to thyroid dysfunction, it can also be explained by the fact that hypothyroid subjects gain weight and conversely hyperthyroid subjects lose weight that ultimately cause significant difference of BMI among various thyroid functional status.

It may be wise to mention here that, some recent past studies by our department (Rajiv *et al.*, 2017 unpublished) revealed that frequency of thyroid autoimmunity is relatively more than is assumed. This is supposed by some to be part of consequences coined by the implementation of universal salt iodization as part of global legislation for iodization of salt. The observed autoimmunity in newly detected diabetic subjects is not part of that phenomenon cannot be claimed clearly until this diabetic subjects are also investigated for the iodine related functional hazards of thyroid. The long term impact of this observation and their consequences need further studies on the matter.

CONCLUSIONS

A comparative study of thyroid hormone levels in diabetic and non-diabetic patients revealed that patients with type-2 DM had significantly lower serum FT3 levels ($p<0.001$) compared to the control groups. There were no significant differences observed in serum FT4 ($p= 0.339$) and TSH ($p= 0.216$) levels between the control and study subjects. In conclusion, present study observed that about 13% of newly diagnosed patient with type-2 DM have thyroid dysfunction with a higher frequency for subclinical hypothyroidism.

REFERENCES

1. Chen, H. S., Wu, T. E., Jap, T. S., Lu, R. A., Wang, M. L., Chen, R. L., & Lin, H. D. (2007). Subclinical hypothyroidism is a risk factor for nephropathy and cardiovascular diseases in Type 2 diabetic patients. *Diabetic medicine*, *24*(12), 1336-1344.
2. Nicholas, A. (2015). Type 2 diabetes mellitus and thyroid dysfunction: an intertwined duo. *African Journal of Diabetes Medicine*, *22*(2), 21-23.
3. Wang, C. (2013). The relationship between type 2 diabetes mellitus and related thyroid diseases. *Journal of diabetes research*, 2013, 1-9.
4. Singh, G., Gupta, V., Sharma, A. K., & Gupta, N. (2011). Evaluation of thyroid dysfunction among type 2 diabetic Punjabi population. *Adv biores*, *2*(2), 3-9.
5. AFKHAMI, A. M., Rashidi, M., & SHOJA, A. A. A. (2010). Effect of thyroid dysfunction on metabolic response in type 2 diabetic patients. *Iranian Journal of Diabetes and Obesity, 2(1), 20-26.*
6. Den Hollander, J. G., Wulkan, R. W., Mantel, M. J., & Berghout, A. (2005). Correlation between severity of thyroid dysfunction and renal function. *Clinical endocrinology*, *62*(4), 423-427.
7. Islam, S., Yesmine, S., Khan, S. A., Alam, N. H., & Islam, S. (2008). A comparative study of thyroid hormone levels in diabetic and non-diabetic patients. *Southeast Asian J Trop Med Public Health*, *39*(5), 913-916.
8. Mukherjee, S. (2015). Prevalence of thyroid dysfunction in young patients with type 2 diabetes mellitus in Eastern India, study of 120 cases from a tertiary care hospital. *Journal of the ASEAN Federation of Endocrine Societies*, *30*(2), 154-154.
9. Hasanat, M. A., Rumi, M. A. K., Alam, M. N., Hasan, K. N., Salimullah, M., Salam, M. A., ... & Khan, A. A. (2000). Status of antithyroid antibodies in Bangladesh. *Postgraduate medical journal*, *76*(896), 345-349.
10. Khuranaa, A., Dhoat, P., & Jain, G. (2016). Prevalence of thyroid disorders in patients of type 2 diabetes mellitus. *J Indian Acad Clin Med*, 17(1), 12-15.