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Abnormal glycemic status is common among adults with thyroid dysfunctions

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Abstract

Background: Abnormal glycemic status and thyroid dysfunctions are the two most common endocrinopathies. Data regarding glycemic status in Bangladeshi patients with thyroid dysfunctions are scarce.

Objective: This study aimed to see the association of glycemic status among patients with thyroid dysfunctions.

Methods: This cross-sectional study was done among 370 adults with thyroid dysfunctions. Serum thyroid stimulating hormone and free thyroxine levels were used to categorize the patients with different thyroid dysfunctions. Fasting plasma glucose for all, two hours after breakfast (2HABF) glucose for previously diagnosed patients with diabetes mellitus (DM) and 75 gm oral glucose tolerance test (OGTT) were analyzed by glucose oxidase method. Glycemic status was defined by American Diabetes Association- 2014 guideline.

Results: The frequency of hypothyroid, subclinical hypothyroid, euthyroid with levothyroxine, subclinical hyperthyroidism, and hyperthyroidism participants were 79 (21.35%), 131 (35.41%), 111 (30.0%), 15 (4.05%) and 34 (9.19%) respectively. There were significant differences in the percentages of glycemic status (p=0.011) among patients with thyroid dysfunctions. The highest percentages of DM and prediabetes were found among patients with subclinical hyperthyroidism (40.0%) and hyperthyroidism (58.82%) respectively. A significant association was found between the duration of thyroid dysfunctions with glycemic status (p=0.037).

Conclusions: Glycemic abnormalities are common in patients with thyroid dysfunctions and require regular screening to prevent mortality and morbidities associated with these combined conditions. *[J Assoc Clin Endocrinol Diabetol Bangladesh, January 2022; 1 (1): 04-08]*

Keywords: Thyroid dysfunctions, Glycemic status, Hypothyroidism, Hyperthyroidism, Diabetes mellitus, Prediabetes

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Introduction

A significant portion of the world population is suffering from different types of thyroid dysfunctions and they are considered the second most common endocrine disorders group.[1,2] Although the prevalence of thyroid dysfunctions is not known in the Bangladeshi population after universal salt iodination, data from our neighboring country India showed a higher prevalence of thyroid dysfunctions in Kolkata especially hypothyroidism (21.67%), subclinical hypothyroidism (11.8%) and 1.5% of hyperthyroidism; considering iodine replete over a decade back which may be similar with Bangladesh iodine status.[3]

The association between diabetes mellitus (DM) and

thyroid dysfunctions is widely known from the first study published in 1979.[4] Thyroid dysfunctions are closely associated with glucose intolerance by various mechanisms including energy homeostasis, pancreatic beta cell function, and insulin resistance.[5] Not only cardiovascular disease but also microvascular complications of DM are associated with thyroid dysfunctions.[6,7] So, patients with thyroid dysfunctions are considered at risk of developing glycemic abnormalities with complications. Early diagnosis and management of glycemic abnormalities in patients with thyroid dysfunctions may reduce the mortality and morbidity associated with these combined clinical identities.

Thyroid dysfunctions among patients with DM are also very common in South Asian countries.[3,8,9] These studies focused on the thyroid dysfunctions among patients with DM. However, there is a lack of studies about the glycemic status among patients with thyroid dysfunctions. This study aimed to see the association of thyroid dysfunctions and their duration with glycemic status.

Materials and Methods

This cross-sectional study was carried out at the Thyroid Clinic of the Department of Endocrinology of a tertiary hospital from 1st July 2014 to 30th June 2015. Adults with different thyroid dysfunctions were consecutively enrolled by a convenient sampling technique. Participants having other endocrine disorders, systemic diseases, and taking any drugs that might affect blood glucose levels as well as clinically suspected cases of thyroiditis, and pregnant and lactating mothers were excluded from the study. The sample size was calculated from the following formula: $n=Z^2pq/d^2$. The prevalence of abnormal glycemic status (p=0.60) in patients with thyroid dysfunctions was taken from a previous study.[10] Considering a 95% level of confidence interval (Z=1.96) with a 10% margin of error (d=0.1), the minimum sample size was 369. We included 370 adults with different thyroid dysfunctions in our study population. The study protocol was approved by the Institutional Review Board of the hospital. The study was conducted according to Helsinki Declaration. Informed written consent was taken from each participant.

Considering both serum thyroid stimulating hormone (TSH, reference value: 0.40 - 4.0 µIU/mL) and free thyroxine (FT4, reference value: 0.8 - 1.8 ng/dl) patients' thyroid status was defined as hypothyroidism, subclinical hypothyroidism, euthyroidism with drugs, subclinical hyperthyroidism, and hyperthyroidism. Along with clinical information, patients with unknown glycemic status were advised to do an oral glucose tolerance test maintaining World Health Organization's guideline to measure fasting (FPG) and 2 hours after 75 gm oral glucose (2H-OGTT). Patients with known cases of DM were advised to do fasting (FPG) as well as two hours after breakfast (2HABF) glucose (mmol/L) from the department of Biochemistry (glucose oxidase method). Glycemic status was defined by American Diabetes Association, 2014 criteria as normal glucose tolerance (NGT), prediabetes, and DM.[11]

Data were entered, coded, and analyzed in a computer by using SPSS (statistical package for social science) version 22.0. Numerical data were expressed in mean ± standard deviation (SD) and qualitative data were expressed in frequency (percent, %). Associations among qualitative variables were tested by Pearson's chi-square test. Associations of numerical variables between groups were analyzed by independent samples t-test. Correlations of numerical variables were done by Pearson's correlation test. A two-sided p-value below 0.05 was considered statistically significant.

Results

Among 370 patients with thyroid dysfunctions, 141 were newly diagnosed and 229 were on medication (213 on levothyroxine and 16 on thionamide). Considering current serum TSH and FT4 values, the frequency of hypothyroid, subclinical hypothyroid, euthyroid with medication, subclinical hyperthyroidism, and hyperthyroidism participants were 79 (21.35%), 131 (35.41%), 111 (30.0%), 15 (4.05%) and 34 (9.19%) respectively. All euthyroid patients were taking levothyroxine (n=111). All 16 patients on thionamide had hyperthyroid status. Hypothyroid patients (new or on levothyroxine) and subclinical hypothyroid patients were considered hypothyroid and others (newly diagnosed hyperthyroid and on thionamide) were considered hyperthyroid patients. A total of 321 had hypothyroidism (86.76%) and 49 had hyperthyroidism (13.24%). On the other hand, 89 patients were previously diagnosed cases of DM.

Both the groups of thyroid dysfunctions had statistically similar ages. The frequency of females was higher with hypothyroidism (87.23% vs. 65.31%, p<0.001) and they had higher BMI (27.89±5.83 vs. 22.92±4.29, kg/m^2, p<0.001) than those with hyperthyroidism. Goiter was statistically more common

among hyperthyroid patients than hypothyroid patients (95.92% vs. 47.35%, p<0.001). All the studied mean plasma glucose values were numerically higher in patients with hyperthyroidism. Among them, only the 2HABF glucose value done among patients with previously diagnosed DM was statistically significant (18.90±3.63 vs. 11.10±3.18, mmol/L, p<0.001) [Table-I].

Glycemic status was significantly different among overall thyroid dysfunctions (p=0.034). The frequency of NGT, PDM, and DM were 136 (42.37%), 92 (28.66%), 93 (28.97%) in patients with hypothyroidism and 15 (30.61%), 23 (46.94%), and 11 (22.45%) in patients with hyperthyroidism respectively. The highest percentages of DM and prediabetes were found among patients with subclinical hyperthyroidism (40.0%) and hyperthyroidism (58.82%) respectively. There were significant differences in the percentages of glycemic status (p=0.011) among patients with thyroid dysfunctions [Figure-1].

A significant association was found between the duration of thyroid dysfunctions with glycemic status (p=0.037). There was a trend of increasing percentages of DM with increasing duration of thyroid dysfunctions, especially after one year of diagnosis [Table-II]. FPG (r=0.119, p=0.022), 2H-OGTT (r=0.121, p=0.040) and 2HABF glucose (r=0.231, p=0.012) had significant positive correlations with FT4 but none with TSH (NS for all) in logarithmic scale [Table-III].

Table-II: Association of the duration of thyroid disease and glycemic status of patients in previously diagnosed patients with thyroid dysfunction (n=229)

Duration of thyroid dysfunctions	No.	Glycemic status			p
		NGT (n=91)	PreDM (n=63)	DM (n=75)	
≤1 year	71	34 (47.9)	24 (33.3)	13 (18.3)	
1.1- 5 years	97	34 (35.1)	23 (23.7)	40 (41.2)	0.037
5.1-10 years	31	15 (48.4)	6 (19.4)	10 (32.3)	
>10 years	30	8 (26.7)	10 (33.3)	12 (40.0)	

NGT (normal glucose tolerance), preDM (prediabetes), DM (diabetes mellitus)
Within parentheses are percentages over row total
Pearson's chi-square test done

Table-III: Correlation of thyroid functions with glycemic values

Determinants of 'r'	No.	log TSH		logFT4	
		r	p	r	p
logFPG	370	-0.084	0.109	0.119	0.022
log2H-OGTT glucose	281	-0.074	0.214	0.121	0.040
log2HABF glucose	89	-0.034	0.324	0.231	0.012

Pearson's correlation test was done

Table-I: Characteristics of the study population (N=370)

Variables	Groups	No.	Hypothyroidism	Hyperthyroidism	p
Age, years	≤30	101	91 (28.35)	10 (20.41)	
	31-40	121	104 (32.40)	17 (34.69)	
	41-50	105	89 (27.73)	16 (32.65)	0.446
	51-60	39	29 (9.03)	3 (6.12)	
	>60	11	8 (2.49)	3 (6.12)	
Sex	Male	58	41 (12.77)	17 (34.69)	<0.001
	Female	312	280 (87.23)	32 (65.31)	
Goiter	Present	199	152 (47.35)	47 (95.92)	<0.001
	Absent	171	169 (52.65)	2 (4.08)	
BMI, kg/m^2		370	27.89±5.83	22.92±4.29	<0.001
Fasting P. glucose, mmol/L		370	5.75±1.89	6.07±2.27	0.696
2H-OGTT glucose, mmol/L		281	7.56±2.54 [321]	8.09±2.12 [40]	0.310
2HABF glucose, mmol/L		89	11.10±3.18 [78]	18.90±3.63 [9]	<0.001

Data were expressed in frequency (%) or mean±SD
Pearson's chi-square test or independent samples t-test was done as appropriate
(Percentages over column total), [available no.], BMI (body mass index), 2HABF (2 hours after breakfast)

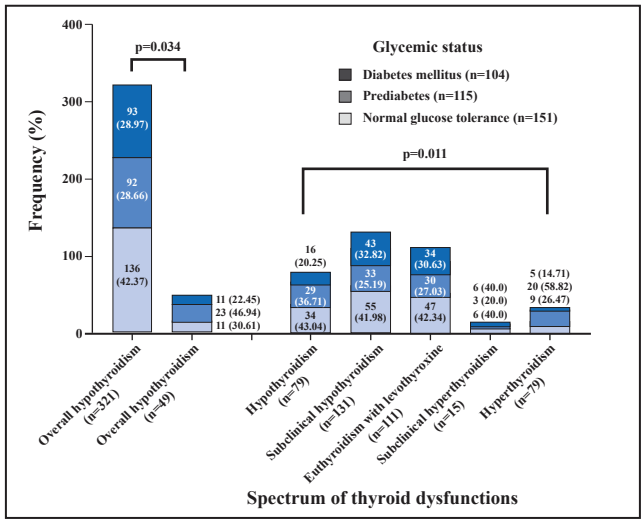

Figure-1: Glycemic status in patients with thyroid dysfunctions (N=370)
Pearson's chi-square test was done

Discussion

This study showed a significant association between thyroid dysfunctions with glycemic status. The percentage of abnormal glycemic status increased with the duration of thyroid dysfunctions. Significant positive correlations were observed with FT4 with different glycemic values.

Around 59.19% (preDM, 31.08%, and DM, 28.11%) of patients with thyroid dysfunctions had abnormal glycemic status. This is similar to the findings observed by Reddy et al. (2014).[10] Among hypothyroid patients, 20.25% had DM and 36.71% had preDM. In a recent publication, 19.41% of hypothyroid patients who had DM attended a general hospital in Bangladesh.[12] Among 65 newly diagnosed thyrotoxic patients, Paul et al. (2004) found glucose intolerance in 72.3% of cases.[13] We also found similar findings (69.89%).

We found significant associations between thyroid dysfunctions with glycemic status. A recent meta-analysis also described a similar observation.[14] Thyroid hormone is diabetogenic. We also found higher blood glucose levels in patients with hyperthyroidism than in hypothyroidism. Similarly, the FT4 level positively correlated with all the glucose values. Despite that, a meta-analysis showed a significant association between subclinical hypothyroidism with type 2 DM. Hyperleptinenmia and insulin resistance may play a role in the association between higher TSH and glucose levels.[15] A recent study from Bangladesh also found a positive correlation between TSH and a negative correlation between FT4 and FT3 with HbA1C among patients with uncontrolled DM.[16]

The prevalence of abnormal glycemic status increased with the duration of thyroid dysfunctions.[17] Over a mean follow-up period of six years, Danish population-based studies showed an increased risk of DM in patients with both hyperthyroid and hypothyroid in comparison to control the population.[18] We also observed a higher percentage of glycemic abnormalities after one year which was similar to the observation by Chen et al. (2019).[19]

The main limitation of our study was its cross-sectional design. However, our sample size was larger than previously described studies from Bangladesh and we approached it differently than previous studies that mostly reported thyroid dysfunctions among patients with DM.

Conclusion

Glycemic abnormalities are common in patients with both hyperthyroidism and hypothyroidism, especially after one year of diagnosis. A further large-scale longitudinal study with periodic follow-up of thyroid dysfunction subjects having normal blood glucose levels might help to reveal the incidence rate of glycemic abnormality in thyroid dysfunctions. Screening for glycemic abnormalities in patients with thyroid dysfunctions may be useful to reduce the long-term complications and mortality associated with these combined conditions.

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Conflict Of Interest
The authors have no conflicts of interest to disclose
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Data Availability
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.
Ethics Approval and Consent to Participate
Ethical approval for the study was obtained from the Institutional Review Board. The written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

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