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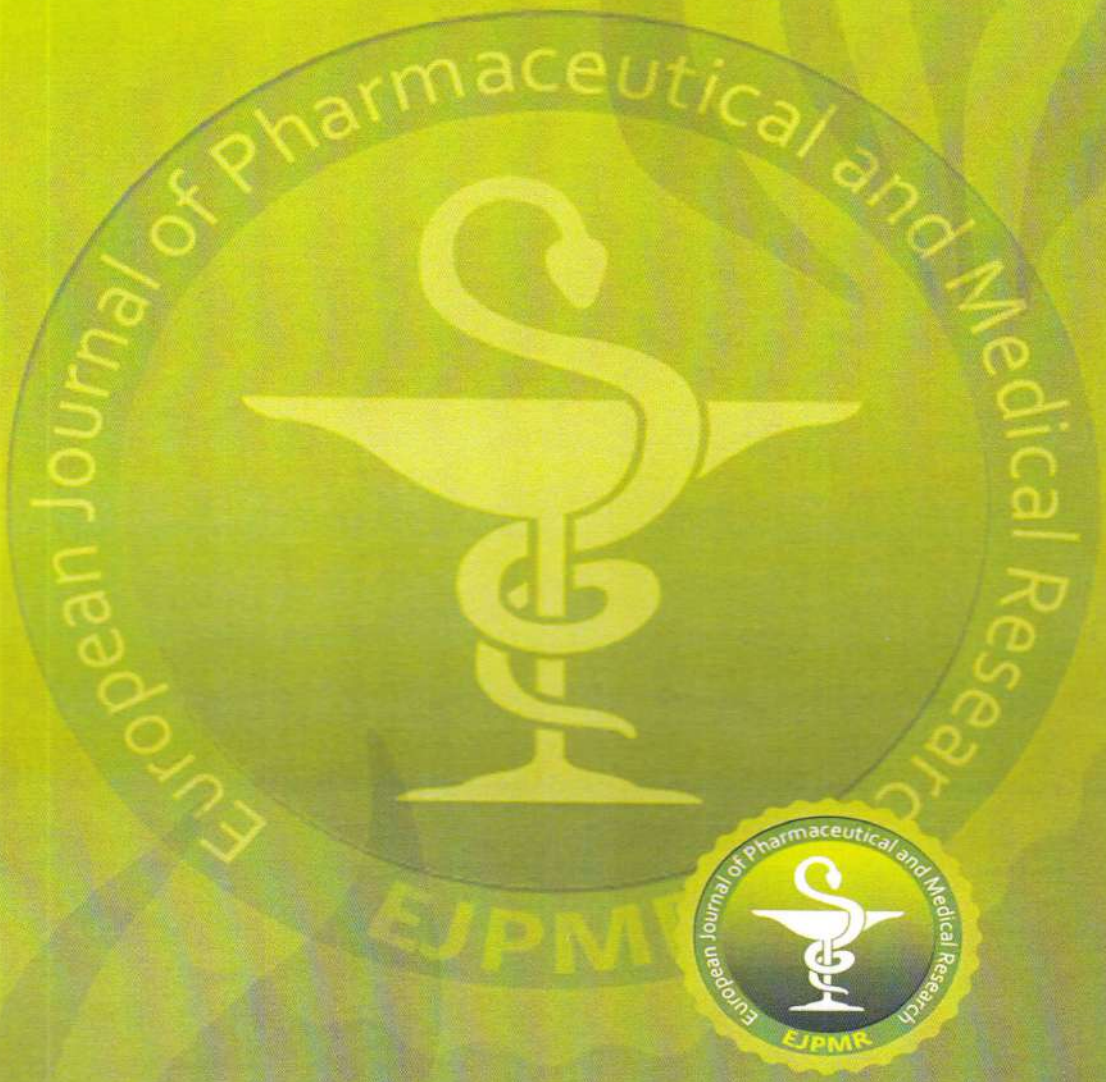
European Journal of Pharmaceutical and Medical Research



Volume 9, Issue 9

Published by
Editor in Chief
EJPMR

EUROPEAN JOURNAL OF
PHARMACEUTICAL AND MEDICAL RESEARCH
Volume 9 Issue 9 September 2022

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ejpmr, 2022,9(8), 21-25

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

FREQUENCY OF THYROID DYSFUNCTION IN NEWLY DETECTED ADULT PATIENTS WITH TYPE 2 DIABETES MELLITUS ATTENDING A TERTIARY CARE HOSPITAL OF BANGLADESH

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Article Received on 06/07/2022 **Article Revised on 26/07/2022** **Article Accepted on 16/08/2022**

ABSTRACT

Background: Thyroid dysfunction and diabetes mellitus (DM) are the two common endocrinopathies but neither causally related nor mutually exclusive. Coexistence of these two conditions is important for management of both the problems. **Objectives:** To see thyroid dysfunction in newly detected type-2 DM. **Materials and 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:** Thyroid dysfunction was observed in 13% subjects. Most of them had subclinical hypothyroidism (8.5%) followed by overt hypothyroidism (3%), subclinical thyrotoxicosis (1.0%) and hyperthyroidism (0.5%). Only 11.5% had family history of thyroid disorder among subjects having dysfunction. About 11% subjects were anti-thyroid antibody positive. 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). **Conclusions:** The results of the present study suggest that the thyroid dysfunction is not uncommon in newly diagnosed type-2 DM. Thyroid autoimmunity is one of the predictors for increased risk of thyroid dysfunction in them. Screening for thyroid dysfunction may be wise in newly diagnosed type-2 DM.

KEYWORDS: Thyroid dysfunction, Diabetes mellitus, Hypothyroidism.

INTRODUCTION

Thyroid dysfunction and diabetes mellitus are the two common endocrinopathies which are neither causally related nor mutually exclusive. Hence coexistence of these two conditions is important in view of covering the management of both the problems. Thyroid dysfunction in patients with diabetes mellitus (DM) is supposed to be higher than general population.[1] But thyroid dysfunction is a graded phenomena, ranging from very mild cases with biochemical abnormalities, without showing any symptoms of thyroid hormone excess or deficiency to very severe cases like life threatening thyrotoxic crisis or myxoedema coma and frequently may be overlooked when associated with diabetes.[2] Patients with thyroid disease usually complain of one or more of the followings: (1) thyroid enlargement, which may be diffuse or nodular; (2) symptoms of thyroid hormone deficiency, or hypothyroidism; (3) symptoms of thyroid hormone excess, or hyperthyroidism; or (4) complications of a specific form of hyperthyroidism—Graves' disease—that may present with striking prominence of the eyes (exophthalmos) and rarely,

thickening of the skin over the lower legs (thyroid dermopathy or pretibial myxedema).[3]

In the Colorado Thyroid Disease Prevalence study involving 25,862 participants attending a state health fair, 9.5% of the studied population were found to have an elevated thyroid stimulating hormone (TSH), while 2.2% had a low TSH.[4] In the National health and nutrition examination survey (NHANES) III study, a survey of 17,353 subjects representing the US population, hypothyroidism was found in 4.6% and hyperthyroidism in 1.3% of subjects.[5] The latter further observed an increased frequency of thyroid dysfunction with advancing age and a higher prevalence of thyroid disease in women compared to men and in subjects with DM. Several reports documented a higher than normal prevalence of thyroid dysfunction in the population with DM. Particularly, Perros et al. demonstrated an overall prevalence of 13.4% of thyroid diseases in patients with DM with the highest prevalence in type-1 DM female (31.4%) and lowest prevalence in type-2 DM male (6.9%).[6] Recently, a prevalence of 12.3% was reported among Greek patients with type-2 DM (Papazafiropoulou 2010).[7] In Saudi patients with type-2 DM 16% were found to have thyroid dysfunction.[8] In Jordan, a study reported that thyroid dysfunction was present in 12.5% of patients with type-2 DM (Radaideh et al. 2004).[8] In addition, positive anti-thyroid peroxidase (TPO) antibodies have been reported in as high as 38% patients with DM and have been shown to be predictive for the development of clinical and subclinical hypothyroidism.

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.[10] 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.

Objective

General

- To observe the frequency of thyroid dysfunction in adult patients with newly detected type-2 DM.

Specific

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

Study design: 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
Sample size determination: Considering 15% dropout the sample size of the study were 200
Sampling method: samples were collected consecutively by purposive sampling technique.

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

The study was carried out during January, 2017 to January, 2018 at department of Endocrinology of BSMMU. Subjects attending with newly diagnosed type-2 DM awaiting were given an appointment after matching inclusion and exclusion criteria. Written consent was taken from each eligible subject after properly explaining the steps and purpose of the study. 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.

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.

RESULTS

This study encompassing 200 subjects with newly diagnosed cases of type-2 DM attending department of Endocrinology of BSMMU intended to see the frequency of thyroid dysfunction. FT4, TSH along with anti-TPO and anti-TG antibodies were done in all 200 study subjects.

Characteristics of the study subjects are shown in table 1 where average age was 41±8.3 years mean±SD, BMI was 26.0±4.2 kg/m^2 mean±SD, and mean WC was 97.3±9.3 cm mean±SD among the study subjects. Around 60% subjects were female, majority of them were from urban areas (78.5%) and nearly half them were housewife (47.5%). 53.5% subjects had a family history of diabetes mellitus while 10.5% had a family history of thyroid disorder. Their blood pressure were within normal limits (mean SBP =132.5±13.2 mmHg and mean DBP=75.2±8.1mmHg mean±SD). 29% subjects were smoker and 38% subjects presented with multiple co-morbidities like hypertension, dyslipidaemia, Ischemic heart disease, stroke etc.

Table 1: Characteristics of the study population (n=200).

Characteristics	Frequency n (%)	Mean±SD
Age (year)		41.1±8.3
BMI (kg/m^2)		26.0±4.2
SBP (mmHg)		132.5±13.2
DBP (mmHg)		75.2±8.1
WC (cm)		97.3±9.3
Gender		
Male	81 (40.5)	
Female	119 (59.5)	
Area of residence		
Urban	157 (78.5)	
Rural	43 (21.5)	
Occupation		
Service	40 (20.0)	
Business	63 (31.5)	
Housewife	95 (47.5)	
Others	2 (1.0)	
Smoking status		
Smoker	58 (29.0)	
Non-smoker	142 (71.0)	
F/H of Diabetes Mellitus		
Yes	107 (53.5)	
No	93 (46.5)	
F/H of Thyroid Disorder		
Yes	21 (10.5)	
No	179 (89.5)	
Co morbidities		
Yes	76 (38.0)	
No	124 (62.0)	

BMI=Body mass index, WC=Waist circumference, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, Co morbidities=Hypertension, Dyslipidaemia, Ischemic Heart Disease, Stroke.

Status of the thyroid function among subjects with diabetes Mellitus and Relation with family history of thyroid disorder

Table 2 describes the thyroid functional status among the study subjects showing 26 (13%) subjects had thyroid dysfunction and table 3 shows the frequency of different subgroups of thyroid dysfunction among the study subjects. Most of them had subclinical hypothyroidism 17 (8.5%) followed by overt hypothyroidism 6 (3%), subclinical thyrotoxicosis 2 (1.0%) and hyperthyroidism 1 (0.5%).

Table 4 displays comparison of family history of thyroid dysfunction with thyroid functional status among study population showing only 3 (11.5%) of the subject with thyroid dysfunction had family history of thyroid disorder whereas a large number of subjects 23 (88.3%) with thyroid dysfunction did not have family history of thyroid disorder though it was not statistically significant.

Table 2: Thyroid functional status among study population (n=200).

Thyroid functional status	Number (n)	Percentage (%)
Euthyroid	174	87
Thyroid dysfunction	26	13
Total	**200**	**100**

Table 3: Subgroups of thyroid dysfunction among study population (n=200).

Categories of dysfunction	Number of patients	Frequency (%) (95% CI)
Hypothyroidism	6	3.0 (0.6-5.4)
Subclinical hypothyroidism	17	8.5 (6.8-9.1)
Hyperthyroidism	1	0.5 (-.5-1.5)
Subclinical thyrotoxicosis	2	1.0 (0.3-2.3)
Total	**26**	**13 (8.4-17.6)**

95% CI=95% Confidence Interval

Table 4: Comparison of family history of thyroid dysfunction with thyroid functional status among study population (n=200).

F/H of thyroid dysfunction	Thyroid dysfunction		P value
	Yes n (%)	No n (%)	
Yes	3 (11.5)	18 (10.3)	0.741
No	23 (88.5)	156 (89.7)	
Total n (%)	**26 (100)**	**174 (100)**	

Within parenthesis are percentages over column total. Analysis done by Fisher's Exact test

Anti-thyroid antibody; relation with thyroid function, HbA1c, level of TSH

Table 5 narrates the frequency of anti-thyroid antibody among the functional groups of thyroid showing 22 (11%) subjects were anti-thyroid antibody positive. Among different subgroups of thyroid functional status most of the overt hypothyroidism (83.3%) and subclinical hypothyroidism (70.6%) were positive for anti-thyroid antibody though the number of subject were smaller. On the contrary euthyroid and hypothyroid subjects were mostly antibody negative (almost cent percent).

Table 5: Frequency of anti-thyroid antibody among study population (n=200)

Thyroid functional status	*Anti-thyroid antibody		Total
	Positive n (%)	Negative n (%)	
Euthyroid	5 (2.9)	169 (97.1)	174
Hypothyroidism	5 (83.3)	1(16.7)	6
Subclinical hypothyroidism	12 (70.6)	5 (29.4)	17
Hyperthyroidism	0	1 (100)	1
Subclinical Thyrotoxicosis	0	2 (100)	2
Total n (%)	22 (11.0)	178 (89.0)	200 (100)

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

DISCUSSION

Present study investigated thyroid dysfunction in newly detected patient with diabetes mellitus in a tertiary level hospital. It was observed that about 13% of the newly diagnosed patients with diabetes mellitus have thyroid dysfunction with a higher frequency for subclinical hypothyroidism followed by hypothyroidism, subclinical thyrotoxicosis and hyperthyroidism. Anti-thyroid antibody was also found to be positive in 11% subjects with highest frequency in subclinical hypothyroidism and overt hypothyroidism. However, 2.9% of euthyroid subjects were also positive for anti-thyroid antibody. Anti-TPO antibody was positive significantly in relatively higher frequency indicating thyroid autoimmunity. Frequency of anti-thyroid antibody was found to be increasing with the increment of TSH level. However, no difference for FT4 and TSH was found for different level of HbA1c and there was observed no particular correlations of glucose level with thyroid hormones and antibody excepting anti-TPO antibody as an impendent predictor for thyroid dysfunction. Similar findings were observed by other investigators in other populations[7]. Therefore, considering the phenomena of global rise of frequency of diabetes, and observation of

autoimmunity among diabetic population by many investigators like us, it may be imperative in future to include testing for thyroid autoimmunity while diagnosing diabetes.

In the present study, 26 (13%) subjects had thyroid dysfunction and 174 (87%) were found to be euthyroid. Similar findings were observed by the investigators in Greek, Portuguese and Jordan population although the study population was from different geographic and ethnic origins.[7] We found subclinical hypothyroidism the commonest dysfunction occurring in 8.5%, followed by overt hypothyroidism in 3.0%, subclinical hyperthyroidism in 1.0% and hyperthyroidism in 0.5%. These results are in concordance with the results of Perros et al. 1995, Celani et al. 1994, Nobre et al. 2008, Chubb et al. 2005, Babu et al. 2001, and Radaiedeh et al. 2004[6,11,12,13,14] It cannot be explained as causally related to diabetes but seems need keep in consideration while diagnosing any subjects as newly detected diabetes as to render the importance of testing for thyroid dysfunction.

In an attempt to find out the status of anti-thyroid antibody in relation with thyroid functional status, 22 (11%) subjects were anti-thyroid antibody positive and among the different subgroups most of the overt hypothyroidism (83.3%) and subclinical hypothyroidism (70.6%) were positive for anti-tyroid antibody. On the other hand, most of the euthyroid (97.1%) and almost all hyperthyroid (100%) subjects were antibody negative. Presence of significantly higher frequency of anti-thyroid auto-antibodies in subjects with type-2 diabetes mellitus indicates important role of autoimmunity in the development of thyroid dysfunction among type 2 diabetes mellitus subjects.[15] Alternatively, the two diseases are prevailing simultaneously in the same population and seems an association though practically are co-occurrence in the same person. Thus unless followed for a substantial period and investigated for causal relation between the two diseases, it cannot be clearly opined about the events. Nevertheless, it does not necessarily mean for presence of one disease in the event of occurrence of another; but warrants for need of searching the presence of one if the other is detected.

CONCLUSION

Newly diagnosed T2DM has zinc level within normal limit. Level of zinc was found to be statistically similar in age groups, glycemic status groups, socioeconomic classes and gender or BMI groups.

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