Spectrum of thyroid function test among type 2 diabetic patients attending a rural health facility, southwest Nigeria: A hospital-based study

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Abstract

Objectives: The thyroid gland produces hormones that have significant influence on carbohydrate metabolism; its disorders may affect carbohydrate metabolism in type 2 diabetic patients (T2DM) more than the non-diabetic (NDM) patients as reported in various studies. We determined the spectrum of thyroid function tests (TFTs) profile among T2DM in our rural health facility.

Methods: T2DM patients and NDM patients were recruited for the study. The age, educational level, occupation, marital status, and duration of diabetes were extracted from interviewer's administered questionnaire. The weight, height, body mass indices (BMIs), and the waist and hip circumferences were measured. Waist-hip ratios (WHR) were calculated for all participants. Venous blood was collected and assayed for free triiodothyronine (fT3), free thyroxine (fT4), and thyroid stimulating hormone (TSH) using a Chemiluminescence Immunoassay (CLIA) 2nd Generation Autoanalyzer. The mean, standard deviation, frequencies, and percentages were calculated for the variables. The student's t-test and chi-square test were also determined as appropriate.

Results: Seventy-eight patients made up of 56 T2DM and 22 NDM were evaluated in this study. Fifty-one were males while 27 were females; 67.9% and 59.1% of the female participants were T2DM and NDM, respectively. The WHR was significantly higher in T2DM than NDM (0.92 ± 0.05 versus 0.88 ± 0.06). The TSH was higher in T2DM than the NDM. Forty-four (78.6%) of the T2DM had euthyroid (normal) biochemical pattern; 12 (21.4%) showed abnormal biochemical pattern of euthyroid sick syndrome, subclinical hyperthyroid, and subclinical hypothyroid. Thirty (53.6%) of the T2DM were diagnosed less than five years ago. The value of TSH was increasing with the duration of diabetes but not in a statistically significant way. None of the T2DM showed overt hypothyroid or hyperthyroid test result.

Conclusion: Thyroid function test may identify diabetics with altered thyroid hormone status that may impact on their metabolic control. Knowledge of the functional state of the thyroid gland can help in achieving a better metabolic control and attenuate the development of complications in T2DM.

Keywords

Thyroid function tests, type 2 diabetes mellitus, rural Nigeria, diabetes management

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Introduction

Diabetes mellitus is a disorder of carbohydrate, fats, and protein metabolism resulting from inadequate or total deficiency of the hormone insulin, either in its secretion or of its metabolic action. Complications which may be acute or chronic with this disease may have significant morbidity as well as mortality. About 463 million adults are living with this condition in the year 2019, with an increasing prevalence of the disorder; 700 million by the year 2045 is projected by the International Diabetes Federation (IDF)[1] estimate.

The associated endocrine gland that can also affect metabolism in the body is the thyroid gland. The thyroid gland hormones play an important role in body metabolism including that of the regulation of carbohydrate metabolism and insulin secreted by the pancreas. Diabetes mellitus is also known to have significant impact on thyroid function. In general, these hormones are closely involved in the metabolism of the body such that any increase or decrease in the level of either hormone can lead to altered functionality of the other. The relationship between the three hormones in homeostasis of carbohydrates, proteins, and lipids metabolism is well documented. Diabetes mellitus affects the thyroid function through the thyroid stimulating hormone (TSH) produced by the pituitary gland; peripheral conversion of thyroxine (T4) to iodothyronine (T3) in tissues such as the kidney and the liver as well as the direct effect of the raised insulin level on the thyroid gland itself.[2,3]

Thyroid disorders affect the well-being of diabetics by adversely impacting on their blood glucose level; this association has been established as far back as 1979 when it was first published.[4] Several studies[5–8] have demonstrated more common occurrence of thyroid dysfunction in T2DM patients than the NDM population.

Assessment of thyroid function may be used to screen for thyroid disorders; confirmation and/or diagnosis of thyroid diseases, as well as monitoring and evaluation of responses to the various treatment modalities. The thyroid stimulating hormone (TSH), total triiodothyronine (TT3) and/or free triiodothyronine (fT3), and total thyroxine and/or free thyroxine (fT4) are usually assayed parameters in the assessment of thyroid function. The diagnostic reliability of thyroid hormone analysis has improved with the introduction of fourth-generation assays for TSH.

Diabetes mellitus with its associated complications is a global cause of increased morbidity and mortality. With a worldwide prevalence, its incidence is increasing, particularly in the developing countries posing a major challenge to public health.[9] Rapid urbanization and economic development had contributed to this increasing incidence. Diabetes mellitus is one of the most common endocrine metabolic disorders. Hyperglycemia in diabetes has a negative effect on thyroid function; therefore, thyroid gland disorder, another endocrine metabolic disease may be a co-pathology in diabetic patients.

Diabetes mellitus is an endocrine disorder which had been shown to affect multiple organs in T2DM including the thyroid gland which may impact negatively on their ability to maintain optimally stable metabolic state. A significant number of type 1 diabetes mellitus (T1DM) demonstrate features of other co-existing autoimmune disorders affecting other organs including the thyroid gland either at the onset or during course of the disease; however, this is not so common in T2DM which is the most prevalent type of diabetes mellitus. Utilization of TFTs for the diagnosis of thyroid diseases is well established. A specific evaluation of our T2DM patients for any abnormality in their thyroid function using TFT performed on an automated chemistry immunoassay analyzer has not been done before in our facility. The objective of this hospital-based prospective descriptive cross-sectional study is to determine the spectrum of thyroid function test profiles among T2DM patients attending the diabetic clinics of our health facility.

Methods

This is a descriptive cross-sectional study conducted at the Federal Teaching Hospital (FTH), Ido-Ekiti, Ekiti State, Nigeria. The institution is one of the two tertiary health facilities in Ekiti State with a bed space of about 350. FTH is in Ido-Ekiti an agrarian community in the Ido/Osi local government area of the state. Ethical approval was obtained from the Health Research Ethics Committee of the Hospital, before starting the study. The prepared consent form was explained and signed by the participants.

The subjects were recruited from the Diabetic Outpatient Clinic of Medicine and General Outpatient Departments (GOPD) of the hospital over a period of 3 months between October 2019 and December 2019. Subjects were recruited after consenting to the study. Paper questionnaire with a face-to-face interview administered by research assistants that were trained on the filling of the questionnaire was used during the recruitment. A pre-test evaluation of the questionnaire was done by principal author with the research assistants on 10 patients at the General Outpatient Department to help understand the translation and other corrections on the questionnaire. Fifty-six (56) subjects were recruited from consenting patients with T2DM in the two diabetic clinics and are on oral antidiabetic agents, while 22 NDM patients from the GOPD were recruited as control for the study.

The inclusion criteria are as follows:

T2DM patients with plasma glucose level of ≤7mmol/L during their last two clinic attendance that fulfilled the following criteria:

- No prior history of thyroid surgery or trauma to the neck;
- No prior exposure to neck irradiation, and
- Gave their consent to participate in the study.

Automatically excluded are as follows:

- Patients with history of neck trauma or surgery;
- Pregnant women;
- Patients with previous exposure to neck irradiation;
- Those with thyroid disorders or medications that affect the thyroid function, and
- Non-consenting patients.

Body weight was measured using the bathroom weighing scale. The heights were measured using a vertical scale portable stadiometer. The body mass indices (BMIs) were calculated based on their weights and heights measured for each participant. A BMI of $< 18.5 \, \text{kg/m}^2$ indicates underweight, between 18.5 and $24.9 \, \text{kg/m}^2$ was normal, overweight was between ≥ 25 and $<30 \, \text{kg/m}^2$ and obesity was $>30 \, \text{kg/m}^2$.

Waist and hip circumferences were measured twice to the nearest centimeter using inelastic, graduated anthropometric tapes, and the mean of both values were recorded. Waist circumference (WC) was measured halfway between the xiphisternum and the umbilicus while hip circumference (HC) was measured at the level of the greater trochanters. The WHR was then computed for each patient. Blood pressure (BP) was measured with a mercury sphygmomanometer. Normal BP was taken as systolic/diastolic of 130/80 mm Hg.

Blood samples for thyroid function test were collected in the morning on their clinic appointment days. Blood samples for each day were submitted at the reception of the chemical pathology laboratory of the hospital for analysis. The collected samples for each clinic day were centrifuged at 3000 g/min for 5 min and the serum collected and stored deep frozen at −20°C until analysis. Analyses of the hormones (TSH, fT4, and fT3) were performed on a second-generation Automated Immunoassay Analyzer–(Autoplex-Gen2 ELISA-CLIA immunoanalyzer) produced by Monobind Inc., 100 North Pointe Drive, Lake Forest, CA 92630, USA, (website: www.monobind.com). The limit of detection for TSH is 0.0062 μIU/mL, for fT3 is 0.742 pg/mL, and for fT4 is 0.28 ng/dL, defined as 2 standard deviation in the measurement of zero doses with this method in our laboratory.

Interpreting the TFT[10,11] the following biochemical patterns were established:

- Primary (overt) hyperthyroidism: Elevated FT3 and/or FT4 with suppressed TSH.
- Subclinical hyperthyroidism: Normal FT3 and/or FT4 with suppressed TSH.
- Primary (overt) hypothyroidism: Suppressed FT3 and/or FT4 with elevated TSH.
- Subclinical hypothyroidism: Normal FT3 and or FT4 with elevated TSH.
- Euthyroid sick syndrome (ESS): Low or normal FT3 and/or FT4 in the presence of normal, low, or high TSH in non-thyroidal sickness.
- Euthyroid: TSH, FT3, and FT4 within normal reference limit.

Statistical analyses

The statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 20. The continuous variables like the age, height, weight, BMI, waist and hip circumference, WHR was summarized as mean and standard deviation using Independent Samples T test and One-way ANOVA as appropriate. The categorical variables like the socio-demographic characteristics were presented as proportion and analyze using Chi-square test with Yates's correction where more than 20% of expected counts were less than 5. Probability (p) value < 0.05 was accepted as statistically significant.

Results

A total of 78 subjects were recruited for this study; 56 were T2DM and 22 were NDM. As shown in Table 1, there were more female (51) than male (27) participants. There were 67.9% and 59.1% of female participants in the T2DM and NDM, respectively. More than 43.6% of the participant had tertiary education and above; about 37.2% of the participants were skilled or professional workers, while close to 70% of the participant were married.

The clinical characteristics of the studied participants are shown in Table 2. The T2DM were older than the NDM subjects but not statistically significant, the WHR among the T2DM was 0.92 ± 0.05 which was significantly higher than the NDM 0.88 ± 0.06; however, there was no significant differences in the BMI of both the T2DM and the NDM. The T2DM had significantly higher BP than the NDM ($136.48 \pm 21.55/78.46 \pm 11.6$ versus $116.36 \pm 11.77/71.36 \pm 6.21$). The TSH was higher among the T2DM but not statistically significant to that of the NDM.

Table 3 shows the spectrum of thyroid function tests (TFTs) of the studied participants. Among the T2DM, 78.6% showed euthyroid (normal) biochemical pattern, while 21.4% showed abnormal biochemical pattern. Of the abnormal pattern, 8.9% were euthyroid sick syndrome pattern, 7.1% were subclinical hyperthyroid pattern, and 5.4% were subclinical hypothyroid. None of the T2DM have overt hypothyroid or hyperthyroid thyroid function test. Only 4.5% of the NDM had abnormal thyroid function test pattern of subclinical hyperthyroid. Out of all the participants, only 13 (T2DM and NDM) were with abnormal TFT pattern, comprising of seven females and six males. There was equal[6] distribution of abnormal TFT pattern between the female and the male T2DM studied. More than 50% of the T2DM patients were diagnosed less than five years ago.

Table 4 shows the mean value of thyroid hormones and the duration of diabetes. The value of TSH was increasing with the duration of diabetes but not statistically significant. The fT3 concentration was also decreasing with increasing duration of diabetes.

Table 1. Sociodemographic characteristics of the studied participants.

Variables	T2DM	NDM	TOTAL	χ^2	p value
	N = 56(71.8%)	N = 22(28.2%)	N = 78(%)		
Gender					
Male	18 (32.1)	9 (40.9)	27 (34.6)	0.536	0.464
Female	38 (67.9)	13 (59.1)	51 (63.4)		
Occupation					
Retired/unemployed	21 (77.8)	6 (22.2)	27 (34.6)	5.988	0.112
Unskilled worker	15 (68.2)	7 (31.8)	22 (28.2)		
Skilled worker	8 (100)	0 (0)	8 (10.3)		
Professional	12 (57.1)	9 (42.9)	21 (26.9)		
Educational status					
None	5 (50)	5 (50)	10 (12.8)	2.062[Y]	0.724
Primary education	10 (76.9)	3 (23.1)	13 (16.7)		
Secondary education	14 (82.4)	3 (17.6)	17 (21.8)		
Tertiary education	25 (73.5)	9 (26.5)	34 (43.6)		
Postgraduate	2 (50)	2 (50)	4 (5.1)		
Marital status					
Single	1 (100)	0 (0)	1 (1.3)	1.962[Y]	0.580
Married	40 (74.1)	14 (25.9)	54 (69.2)		
Divorced	4 (100)	0 (0)	4 (5.1)		
Widowed	11 (57.9)	8 (42.1)	19 (24.4)		

Abbreviations: T2DM: type 2 diabetes mellitus; NDM: non-diabetes mellitus; χ^2: Chi-square test; Y: Yates-corrected Chi-square test.

Table 2. Anthropometric and clinical characteristics of the studied participants.

Characteristics	T2DM	NDM	p-value
	Mean ± SD	Mean ± SD	
Age (years)	61.32 ± 11.94	59.50 ± 14.45	0.570
Weight(kg)	73.50 ± 13.22	71.27 ± 14.14	0.512
Height (m)	1.62 ± 0.9	1.60 ± 0.06	0.917
Body mass index (kg/m^2)	28.20 ± 4.97	28.07 ± 5.99	0.922
Waist circumference (cm)	96.65 ± 9.70	91.44 ± 13.16	0.058
Hip circumference (cm)	105.66 ± 11.81	104.37 ± 14.73	0.686
Waist–hip ratio	0.92 ± 0.05	0.88 ± 0.06	0.004*
Systolic blood pressure (mm Hg)	136.48 ± 21.55	116.36 ± 11.77	0.001*
Diastolic blood pressure (mm Hg)	78.46 ± 11.6	71.36 ± 6.21	0.008*
Thyroxine stimulating hormone (μIU/mL)	1.52 ± 1.27	1.24 ± 0.84	0.343
Free T4 (ng/dL)	1.05 ± 0.23	1.06 ± 0.30	0.875
Free T3 (pg/mL)	2.22 ± 0.44	2.17 ± 0.45	0.655

Abbreviations: T2DM: type 2 diabetes mellitus; NDM: non-diabetes mellitus; SD: standard deviation.
*Statistically significant.

Discussion

In our study, the TSH level and the thyroid hormones in T2DM patients were not statistically different from the NDM although the concentration of TSH was higher in the T2DM. This finding is similar to what Udiong found among diabetic subjects in Calabar, Nigeria, where the mean TSH value in the diabetics was not significantly higher than the controls.[12] In Southeast Asia, Islam et al.[13] also did not find any significant differences in TSH level among diabetics and non-diabetics. The thyroid hormones are known antagonist of insulin and thyrotrophin releasing hormone (TRH) synthesis is decreased in diabetes mellitus. These factors may be responsible for the occurrence of low concentration of thyroid hormones in diabetic patients.

Overall, 21.4% of the diabetics had abnormal thyroid function tests, this is slightly lower than that in Ibadan where 29.7% was found by Ghazali and Abbiyesuku.[14] Only 4.5% of the NDM had abnormal thyroid function tests while in Ibadan, 2.8% of the controls have thyroid dysfunction. In

Table 3. Spectrum of the thyroid function test profile of the studied participants.

Thyroid function test profile	Sex	T2DM	NDM	Total	χ^2	*p* value
Euthyroid	Male	12	9	21	1.380[Y]	0.926
	Female	32	12	44		
	Total	44 (78.6)	21 (95.5)	65		
Subclinical hyperthyroid	Male	2	0	2		
	Female	2	1	3		
	Total	4 (7.1)	1 (4.5)	5		
Subclinical hypothyroid	Male	1	0	1		
	Female	2	0	2		
	Total	3 (5.4)	0 (0)	3		
Euthyroid sick syndrome	Male	3	0	3		
	Female	2	0	2		
	Total	5 (8.9)	0 (0)	5		

Abbreviations: T2DM: type 2 diabetes mellitus; NDM: non-diabetes mellitus; χ^2: Chi-square test; Y: Yates-corrected Chi-square test.

Table 4. Duration of DM and thyroid function test (TFT).

TFT	Duration of DM in years			F	*p* value
	< 5 years n = 30 (53.6%)	> 5 years–< 10 years n = 15 (26.8%)	> 10 years n = 11 (19.6%)		
TSH	1.45 ± 1.19	1.52 ± 1.36	1.71 ± 1.44	0.617	0.544
FT4	1.08 ± 0.21	0.98 ± 0.29	1.06 ± 0.22	0.923	0.404
FT3	2.29 ± 0.49	2.18 ± 0.33	2.11 ± 0.45	0.636	0.533

Abbreviations: TFT: thyroid function test; TSH: thyroid stimulating hormone; FT4: free thyroxine; FT3: free triiodothyronine; DM: diabetes mellitus; F: F test.

Enugu, using the combination of TSH, fT3, and fT4 levels, Ogbonna and Ezeani[15] found a prevalence of 12.4% among the T2DM patients to have thyroid dysfunction. Other studies outside Nigeria have varied prevalence of thyroid dysfunction among diabetic patients. In northeast India, a similar study involving 80 participants, a prevalence of 30% was found among the diabetics' subjects.[16] Similarly, a prevalence of 12.3% was reported among Greek diabetic patients and 16% of Saudi patients with T2DM were found to have thyroid dysfunction.[6,7] In Jordan thyroid dysfunction was present in 12.5% of T2DM patients.[8] The variability in the prevalence rates may be due to the number of subjects that were used for the various studies. In our study, the national prevalence rate of diabetes mellitus was not used to calculate the number of subjects appropriate for our study. The T2DM patients in our study were selected based on the blood glucose level of ⩽7mmol/L on that clinic day with records in their last previous clinic attendance that shows blood glucose level of ⩽7mmol/L and met the other stated criteria.

The spectrum of thyroid function statuses found in our study includes euthyroid, subclinical hyperthyroid, subclinical hypothyroid, and euthyroid sick syndrome. There was no overt hypothyroid or overt hyperthyroid in our studied T2DM patients. In our study, 78.6% of our T2DM patients were euthyroid showing all parameters within the reference ranges. Subclinical hyperthyroidism was found in 7.1 % of the T2DM cases, and subclinical hypothyroidism was found in 5.4% of them. The remaining 8.9% had euthyroid sick syndrome. Alterations in thyroid hormone levels of varying degree in T2DM have also being found in multiple studies.[17–19] Recent studies have also demonstrated that subclinical hypothyroidism is more common in T2DM. An increased prevalence of thyroid dysfunction was found during clinical evaluations, though not statistically significant, still supports the need to screen for thyroid dysfunction in diagnosed T2DM patients.[20–22] Subclinical hyperthyroidism has also been found in T2DM, though in fewer numbers than subclinical hypothyroidism. So, it may be necessary to screen for both disorders routinely in T2DM[23,24]. Although generally, subclinical hypothyroidism has higher prevalence in comparison to subclinical hyperthyroidism.

T2DM are on various types of oral antidiabetic medications that may be accountable for the alteration in their thyroid hormone levels. For instance, metformin has been found to be associated with reduction in level of TSH without significant associated changes in fT4 and fT3 concentration in several different studies. This finding has been reported in T2DM patients with primary hypothyroidism both under replacement therapy and untreated.[25–27] In our facility, majority of our patients are on metformin and sulfonylureas. The mean TSH of T2DM in our study was within the reference level but slightly higher than the NDM. This may also be accounted for by the number of subjects we studied and the fact that we had lesser number of NDM than the T2DM.

Changes in thyroid hormones levels have been described in patients with diabetes particularly in those with poor plasma glucose control. In diabetic patients, the nocturnal TSH peak is blunted or abolished, and the TSH response to TRH is impaired.[28] Alteration in TFTs may reflect changes in production of thyroid hormones by the effects of hyperglycemia on thyroid gland, on the hypothalamic-pituitary-thyroid axis, and/or on peripheral tissue metabolism of the hormones, or by combination of these effects. The hormones fT3 and fT4 are insulin antagonists that potentiate the action of insulin indirectly.[29] TRH synthesis also decreases in diabetes mellitus.[18,30] These facts could be responsible for the occurrences of low thyroid hormone levels in some diabetics.

In our study, the majority of the T2DM patients had duration of diabetes up to 5 years; no relationship was found between the duration of diabetes and thyroid dysfunction; however, the values of the TSH were increasing over the period of the diabetes. Other similar studies did not find any significant relationship between duration of diabetes and thyroid dysfunction.[31,32] In Enugu, however, Ogbonna and Ezeani[15] reported that the duration of diabetes >5 years was a risk factor for thyroid dysfunction. Other studies have also found a relationship between the duration of diabetes >5 years and thyroid disorders.[33–35]

The mean BP for the T2DM subjects was 136.5 systolic and 78.5 diastolic compared to the NDM of 116.4 systolic and 71.4 diastolic. This agrees with Zimmet et al.[36] and many other studies which reported an increased prevalence of hypertension in type 2 diabetics.

In the socio-demographic characteristics of the studied subjects, there were more females than male participants in both T2DM and NDM, a similar finding in recent studies.[22,37,38] Diabetes and obesity occurring together have been widely reported to be more prevalent in the female population than the male.[39,40]

There were more unemployed/unskilled workers with diabetes than the skilled professional workers. This rural community is an agrarian environment, thus not surprising that more unskilled workers have diabetes. The tertiary health institutions located in the community may account for the skilled/professional workers. The educational status was equally distributed between the tertiary/professional T2DM and the secondary and lower education T2DM. Although these are not significant, however, it is well established by various studies that socioeconomic status (SES) influences the prevalence and complications of diabetes mellitus.

The SES is a total measure of an individual's or families economic and social position.[41–43] Among the SES factors, gender, age, marital status, level of education, income, occupation, region, residential area, the amount of remaining debt, and current liability are associated with diabetes.[44,45] Each of these factors provides information regarding association of risks and identifying their effects which helps in understanding and addressing the socioeconomic inequalities in diabetes. Despite the association of low SES and educational level with the prevalence of diabetes mellitus,[46] controversy still exists whether diabetes is a disease of low SES or high SES or there is no relationship between them.[47] A study in Thailand concluded that low educational attainment with other SES factors was significantly associated with diabetes in Thais.[48]

Limitations

Our study did not use any formulae to calculate the study population and the duration of the study was limited due to the pandemic that occurred with suspension of clinic attendance for more than one year. The cost of maintaining the blood samples viability and that of the reagents prompted for an early analysis of the blood samples. The thyroid hormones were analyzed using an automated chemistry immunoassay analyzer; however, the sample analysis was not done in duplicates or repeated.

Conclusion

The association between diabetes mellitus and thyroid disorders is characterized by a complex interdependent interaction. Thyroid function test in diabetes may identify those that have altered thyroid function for early review and management. Unidentified thyroid dysfunction may distort the metabolic controls in patients with diabetes. The early recognition and treatment of thyroid disorder in diabetic patients may benefit plasma glucose control, attenuate cardiovascular risk, and improve general well-being.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval for this study was obtained from the Health Research Ethics Committee of the Federal Teaching Hospital, Ido-Ekiti, (ERC/2019/02/20/191B).

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References

1. International Diabetes Federation. IDF diabetes atlas, 2019, https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html (accessed 10 September 2020).
2. Ray S and Ghosh S. Thyroid disorders and diabetes mellitus: double trouble. *J Diabetes Res Ther* 2016; 2: 1–7.
3. Nair A, Jayakumari C, Jabbar PK, et al. Prevalence and associations of hypothyroidism in Indian patients with type 2 diabetes mellitus. *J Thyroid Res* 2018; 2018: 5386129.
4. Feely J and Isles TE. Screening for thyroid dysfunction in diabetics. *Br Med J* 1979; 1: 1678.
5. Perros P, McCrimmon RJ, Shaw G, et al. Frequency of thyroid dysfunction in diabetic patients: value of annual screening. *Diabet Med* 1995; 12(7): 622–627.
6. Papazafiropoulou A, Sotiropoulos A, Kokolaki A, et al. Prevalence of thyroid dysfunction among Greek type 2 diabetic patients attending an outpatient clinic. *J Clin Med Res* 2010; 2: 75–78.
7. Akbar DH, Ahmed MM and Al-Mughales J. Thyroid dysfunction and thyroid autoimmunity in Saudi type 2 diabetics. *Acta Diabetol* 2006; 43(1): 14–18.
8. Radaideh AR, Nusier MK, Amari FL, et al. Thyroid dysfunction in patients with type 2 diabetes mellitus in Jordan. *Saudi Med J* 2004; 25(8): 1046–1050.
9. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. *Lancet* 2016; 387: 1513–1530.
10. Dayan CM. Interpretation of thyroid function tests. *Lancet* 2001; 357: 619–624.
11. Carvalho GA, Perez CL and Wards LS. The clinical use of thyroid function tests. *Arq Bras Endocrinol Metab* 2013; 3: 193–204.
12. Udiong CEJ, Udoh AE and Etukudoh ME. Evaluation of thyroid function in diabetes mellitus in Calabar, Nigeria. *Indian J Clin Biochem* 2007; 22(2): 74–78.
13. Islam S, Yesmine S, Khan SA, et al. Comparative study of thyroid hormone levels in diabetic and non-diabetic patients. *Southeast Asian J Trop Med Public Health* 2008; 39(5): 913–916.
14. Ghazali SM and Abbiyesuku FM. Thyroid dysfunction in Nigerian type 2 diabetic patient. *Nig J Physiol Sci* 2010; 25: 176–179.
15. Ogbonna SU and Ezeani IU. Risk factors of thyroid dysfunction in patients with type 2 diabetes mellitus. *Front Endocrinol* 2019; 10: 440.
16. Chutia H, Bhattacharyya H, Ruram AA, et al. Evaluation of thyroid function in type 2 diabetes in northeastern part of India: a hospital-based study. *J Family Med Prim Care* 2018; 7: 752–755.
17. Smithson MJ. Screening for thyroid dysfunction in a community population of diabetic patients. *Diabet Med* 1998; 15(2): 148–150.
18. Suzuki J, Nanno M, Gemma R, et al. The mechanism of thyroid hormone abnormalities in patients with diabetes mellitus. *Nippon Niabunpi Gakki Zasshi* 1994; 70(4): 465–470.
19. Celani MF, Bonati ME and Stucci N. Prevalence of abnormal thyrotropin concentrations measured by a sensitive assay in patients with type 2 diabetes mellitus. *Diabetes Res* 1994; 27(1): 15–25.
20. Maxzud MC, Rasjido LG, Calafiore FA, et al. Prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus. *Medicina* 2016; 76: 355–358.
21. Palma CC, Pavesi M, Nogueira VG, et al. Prevalence of thyroid dysfunction in patients with diabetes mellitus. *Diabetol Metab Syndr* 2013; 5: 58.
22. Ozair M, Noor S, Raghav A, et al. Prevalence of thyroid disorders in North Indian type 2 diabetic subjects: a cross sectional study. *Diabetes Metab Syndr* 2018; 12: 301–304.
23. Khatiwada S, Sah SK, Kc R, et al. Thyroid dysfunction in metabolic syndrome patients and its relationship with components of metabolic syndrome. *Clin Diabetes Endocrinol* 2016; 2: 3.
24. Demitrost L and Ranabir S. Thyroid dysfunction in type 2 diabetes mellitus: a retrospective study. *Indian J Endocrinol Metab* 2012; 16(Suppl. 2): S334–S335.
25. Vigersky RA, Filmore-Nassar A and Glass AR. Thyrotropin suppression by metformin. *J Clin Endocrinol Metab* 2006; 91: 225–227.
26. Isidro ML, Penín MA, Nemiña R, et al. Metformin reduces thyrotropin levels in obese, diabetic women with primary hypothyroidism on thyroxine replacement therapy. *Endocrine* 2007; 32(1): 79–82.
27. Cappelli C, Rotondi M, Pirola I, et al. TSH-lowering effect of metformin in type 2 diabetic patients: differences between euthyroid, untreated hypothyroid, and euthyroid on L-T4 therapy patients. *Diabetes Care* 2009; 32: 1589–1590.
28. Gursoy NT and Tuncel E. The relationship between the glycemic control and the hypothalamus-pituitary-thyroid axis in diabetic patients. *Turk J Endocrinol Metab* 1999; 4: 163–168.
29. Granner DK. Thyroid hormones. In: Murray RK, Granner DK, Mayes PA, et al. (eds) *Harper's biochemistry*. 25th ed. London: Prentice-Hall International Inc., 2000, pp. 533–538.
30. De Greef WJ, Rondeel JM, Van-Haasteren GA, et al. Regulation of TRH production and release in rats. *Acta Med Austria* 1992; 19: 77–79.
31. Diez JJ, Sanchez P and Iglesias P. Prevalence of thyroid dysfunction in patients with type 2 diabetes. *Exp Clin Endicrinol Diabetes* 2011; 119: 201–207.
32. Ravishankar SN, Champakamalini, Venkatesh, et al. A prospective study of thyroid – dysfunction in patients with type 2 diabetes in general population. *Arch Med* 2013; 5: 2.
33. Telwani AA, Wani ZH, Ashraf Y, et al. Prevalence of thyroid dysfunction in type 2 diabetes mellitus: a case control study. *Int J Res Med Sci* 2017; 5: 4527–4531.
34. Sreelatha M, Kumar VS, Shekar GC, et al. Study of thyroid profile in patients with type 2 diabetes mellitus. *Int J Sci Stud* 2017; 5: 211–220.

35. Al-Lehibi KI, Abdulraham MI and Albassam AE. Thyroid dysfunction in type 2 diabetic patients and the effect of diabetes duration and anti-glycemic medications on mean TSH and A1c levels: a retrospective study. *Int J Med Res Health Sci* 2019; 8: 117–122.
36. Zimmet P, Alberti KG and Shaw J. Global and societal implications of the diabetes epidemic. *Nature* 2001; 414: 782–787.
37. Jali MV, Kambar S, Jali SM, et al. Prevalence of thyroid dysfunction among type 2 diabetes mellitus patients. *Diabetes Metab Syndr* 2017; 11: S105–S108.
38. Witting V, Bergis D, Sadet D, et al. Thyroid disease in insulin-treated patients with type 2 diabetes: a retrospective study. *Thyroid Res* 2014; 7: 2.
39. Okosun IS, Forrester TE, Rotimi CN, et al. Abdominal adiposity in six populations of West Africa descent: prevalence and population attributable fraction of hypertension. *Obes Res* 1999; 7: 453–462.
40. Scavini M, Stidley CA, Shah VO, et al. Prevalence of diabetes is higher among female than male Zuni Indians. *Diabetes Care* 2003; 26(1): 55–60.
41. Hu FB. Globalization of diabetes: the role of diet, lifestyle, and genes. *Diabetes Care* 2011; 34(6): 1249–1257.
42. World Health Organization. Noncommunicable diseases and mental health. *United Nations high-level meeting on noncommunicable disease prevention and control*, 2011, https://www.un.org/en/ga/ncdmeeting2011/documents.shtml (accessed 8 May 2022).
43. Secretary's Advisory Committee. Healthy people 2020: an opportunity to address societal determinants of health in the U.S. *report of the secretary's advisory committee on national health promotion and disease prevention objectives for* 2020, 2010, https://www.healthypeople.gov/2020/About-Healthy-People/History-Development-Healthy-People-2020/Advisory-Committee
44. Hwang J and Shon C. Relationship between socioeconomic status and type 2 diabetes: results from Korea National Health and Nutrition Examination Survey (KNHANES) 2010–2012. *BMJ Open* 2014; 4: 005710.
45. Thomas C, Nightingale CM, Donin AS, et al. Socio-economic position and type 2 diabetes risk factors: patterns in UK children of South Asian, Black African-Caribbean and White European origin. *PLoS ONE* 2012; 7(3): e32619.
46. Berkowitz SA, Karter AJ, Lyles CR, et al. Low socioeconomic status is associated with increased risk for hypoglycemia in diabetes patients: the Diabetes Study of Northern California (DISTANCE). *J Health Care Poor Underserved* 2014; 25(2): 478–490.
47. Adler NE and Newman K. Socioeconomic disparities in health: pathways and policies. *Health Aff* 2002; 21(2): 60–76.
48. Suwannaphant K, Laohasiriwong W, Puttanapong N, et al. Association between socioeconomic status and diabetes mellitus: the national socioeconomics survey, 2010 and 2012. *J Clin Diagn Res* 2017; 11: LC18–LC22.