PATTERN OF THYROID DYSFUNCTION AMONG DIABETIC AND HYPERTENSIVE PATIENTS IN KANO METROPOLIS

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ABSTRACT
Background: Studies have associated thyroid dysfunction with diabetes and hypertension, two non-communicable diseases, the burden of which continues to increase in Sub-Saharan Africa. However, information is scanty on the prevalence of thyroid dysfunction among diabetics and hypertensives in Kano.
Aim: The study determined the pattern of thyroid dysfunction among diabetic and hypertensive patients in Kano metropolis.
Methods: The levels of serum fT3, fT4 and TSH in diabetic, hypertensive patients and control were determined and expressed as Mean±SD. A total of 120 participants were involved in the study with 47 being diabetic patients, 43 hypertensive patients and 30 healthy individuals served as control.
Results: The serum TSH, fT4 and fT3 of the diabetic group was found to be 2.33 ± 3.64, 16.85 ± 3.10 and 2.49 ± 0.68 respectively. The serum TSH, fT4 and fT3 of the hypertensive group was found to be 1.78 ± 1.30, 13.4 ± 2.35 and 2.40 ± 0.47respectively. The serum TSH, fT4 and fT3 of the control group was found to be 2.84 ± 1.28, 11.17 ± 1.93 and 2.37 ± 0.17 respectively. This represent a significant difference in fT4 levels between the diabetic and control group, and a significant difference in fT4 and TSH levels between the hypertensive group and control group. The prevalence rate of thyroid dysfunction in diabetics was found to be 6.38% with 4.25% accounted for by subclinical hypothyroidism and 2.13% were filed under Sick Euthyroid. In hypertensives, the prevalence was found to be 6.98%; 4.65% of cases were classified as Sick Euthyroid and only 2.33% was accounted for by Subclinical hypothyroidism. In the control group, the prevalence rate of thyroid dysfunction in diabetics was found to be 6.67% with 2.50% of that due to subclinical hypothyroidism and 4.17% due to Sick Euthyroid cases.
Conclusion: This study proves that the prevalence of thyroid dysfunction was higher in Diabetics and Hypertensives than in apparently healthy people.
Keywords: Hypertension, Diabetes Mellitus, Thyroid hormone, FT3, fT4

INTRODUCTION

The thyroid gland is an endocrine gland at the front of the neck, just below the Adam's apple. The thyroid gland secretes three hormones; the two thyroid hormones (thyroxine/T4 and triiodothyronine/T3), and calcitonin. The thyroid hormones have metabolic, cardiovascular and developmental effects. The thyroid may be affected by several diseases. An excessive secretion of the thyroid hormones by the thyroid gland is called hyperthyroidism, mostly caused by Grave's disease, an autoimmune disorder. In contrast, hypothyroidism is a state of insufficient thyroid hormone production. Globally, the most common cause is iodine deficiency. Thyroid hormones are important for development, and hypothyroidism secondary to iodine deficiency remains the leading cause of preventable intellectual disability (Longo *et al.,* 2011). Diabetes mellitus (DM), popularly referred to as diabetes, is characterized by hyperglycemia (high blood glucose levels) over a prolonged period (Colledge *et al.,* 2010).

Symptoms of high blood sugar level include polyuria (frequent urination), polydypsia (increased thirst), and polyphagia (increased hunger) (WHO, 2013). If left untreated, diabetes can cause many complications. Acute complications may include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and damage to the eyes (WHO, 2013).

Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced. Hypertension (HTN or HT), also known as high blood pressure (HBP), is a long-term medical condition in which the blood pressure in the arteries is persistently elevated (Naish and Court, 2014). Long-term high blood pressure is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral arterial disease, vision loss, chronic kidney disease, and dementia.

Hypertension can be classified as either primary (essential) high blood pressure or secondary high blood pressure (Poulter *et al.,* 2015). Primary hypertension which accounts for up to 95% of cases is defined as high blood pressure due to nonspecific lifestyle and genetic factors (Poulter *et al.,* 2015). The remaining 5–10% of cases are categorized as secondary high blood pressure due to an identifiable cause, such as chronic kidney disease, narrowing of the kidney arteries, an endocrine disorder, or the use of birth control pills.

Thyroid hormones are intimately involved in cellular metabolism (Reinehr, 2013). Thus, excess or deficit of either insulin or thyroid hormones could result in the functional derangement of the cellular metabolism. Thyroid disorders have a major effect on the regulation of glucose. When thyroid dysfunction ensues, the glucose homeostatic balance is broken. Insulin resistance, mainly associated with increased hepatic gluconeogenesis, is characteristic of an excess of thyroid hormones and explains why glucose control deteriorates when diabetic patients develop hyperthyroidism (Brenta, 2010).

In patients with hypertension, structural change of vascular tissue and alteration in the autonomic nervous system by thyroid hormone deficiency may increase total peripheral vascular resistance and hypothyroidism. Hypothyroid patients have also shown reduced dopaminergic activity in central nervous system that increases the norepinephrine level, which further contributes to the development of hypertension. The aim of this study was to investigate the prevalence and pattern of thyroid dysfunction in diabetics, and hypertensives and compare this with the control group.

MATERIALS AND METHODS

Study Population

The study participants were divided into three groups.

Group A (Test Group)

The first group contained 47 known diabetic patients previously diagnosed to have type 2 diabetes who were on management at Murtala Muhammad Specialist Hospital.

Group B (Test Group)

Group B contained 43 known hypertensives patients previously diagnosed to have Hypertension and are currently on management and follow up at Hypertensive outpatient clinic of Murtala Muhammad Specialist Hospital

Group C (Control Group)

The third group consisted of 30 apparently healthy individuals who served as the control group.

Criteria for diagnosis of thyroid dysfunction

Subjects were stratified into one of the following five groups based on the result of their thyroid profile tests.

Table 1: Criteria for diagnosis of thyroid dysfunction

Thyroid function	TSH	fT4	fT3
Euthyroid	0.28 – 6.82 µIU/ml (NORMAL)	10.32 – 25.80 pmol/L (NORMAL)	2.15 – 6.45 pmol/L (NORMAL)
Sick Euthyroid	0.28 – 6.82 µIU/ml (NORMAL)	< 10.32 (LOW)	2.15 – 6.45 pmol/L (NORMAL)
Subclinical hypothyroidism	> 6.82 (HIGH)	10.32 – 25.80 pmol/L (NORMAL)	2.15 – 6.45 pmol/L (NORMAL)
Clinical hypothyroidism	> 6.82 (HIGH)	< 10.32 (LOW)	<2.15 (LOW)
Secondary hypothyroidism	< 0.28 (LOW)	<10.32 (LOW)	< 2.15 (LOW)
Subclinical Hyperthyroidism	< 0.28 (LOW)	10.32 – 25.80 pmol/L (NORMAL)	2.15 – 6.45 pmol/L (NORMAL)
Clinical Hyperthyroidism	< 0.28 (LOW)	> 25.80 (HIGH)	> 6.45 (HIGH)
Secondary Hyperthyroidism	> 6.82 (HIGH)	> 25.80 (HIGH)	> 6.45 (HIGH)

Source: Nwokolo *et al*., 2014, reference ranges were obtained from Accubind™, ELISA kit

Sample Analysis

Five (5) milliliter of blood was collected from peripheral vain (antecubital venipuncture) with minimal application of tourniquet after cleaning the skin with methylated spirit. Sterilized 5ml syringes with 22-G needle were used. Plasma for biochemical estimation was obtained by centrifugation at 3500rpm for 5minutes. Thyroid Hormone levels was then assayed using Sandwich enzyme immunoassay (Accu-bind ELISA micro well).

Statistical Analysis

Data was summarized and entered into a Microsoft Excel 2013 worksheet. The summarized data was checked and cleared of errors using the triangulation tool. The data was then analyzed using Statistical Package for the Social Sciences (SPSS) for windows version 20.0 and Graphpad Prism for windows version 7.02 software applications. All data were expressed as mean ± standard deviation (SD).

An independent t-test was used to evaluate the differences between mean serum levels of thyroid hormones between the test groups and the control group. A p value < 0.05 was considered significant at 95% confidence interval.

RESULTS

General Characteristics

A total of 120 participants were included in this study. They were divided into groups A, B and C. Group A and B comprised of 47 and 43 diabetics and hypertensives respectively who served as the test group while Group C consisted of 30 apparently healthy people who served as the control group.

All test patients presented with a history of diabetes or hypertension in diabetic and hypertensive clinics. The mean ± standard deviation (SD) age was found to be 54.02 ± 13.55 for diabetic patients, 51.84 ± 12.56 for hypertensive patients and 39.03 ± 15.60 for the control group with a range of 21– 80 years. The mean age is represented in Table 2 below.

Table 2: The Mean Age of Respondents

	Diabetic patients	Hypertensive patients	Healthy Control
	Mean ± S. D	Mean ± S. D	Mean ± S. D
Age	54.02 ± 13.55	51.84 ± 12.56	39.03 ± 15.60

Serum Level of Thyroid Hormones in Patients and Control Group

The results of the thyroid hormone levels across different groups is represented in Table 3 below. Both diabetics and hypertensives showed significant increase in fT4 levels when compared to the control group. fT3 and TSH levels were not significantly different when diabetic respondents were compared with the control group. This is in marked contrast to hypertensive patients who still showed significant difference in TSH levels between them and the control group. The findings are represented in Table 4 and 5 respectively.

Table 3: Serum level of Thyroid Hormones in Diabetic patients, Hypertensive patients and control groups

	Diabetic	Hypertensive	Healthy Control
	Mean ± S. D	Mean ± S. D	Mean ± S. D
TSH (µIU/ml)	2.33 ± 3.64	1.78 ± 1.30	2.84 ± 1.28
fT4 (pmol/L)	16.85 ± 3.10	13.4 ± 2.35	11.17 ± 1.93
fT3 (pmol/L)	2.49 ± 0.68	2.40 ± 0.47	2.37 ± 0.17

TSH= Thyroid stimulating hormone, fT3= triiodothyronine
fT4= thyroxine

Table 4: Comparison of Thyroid function tests between DM patients and Control

	DM	Healthy control	
	Mean ± S. D	Mean ± S. D	P value
TSH	2.33 ± 3.64	2.84 ± 1.28	0.465
fT4	16.85 ± 3.10	11.10 ± 1.93	0.000*
fT3	2.49 ± 0.68	2.37 ± 0.17	0.373

*=significant
TSH= Thyroid stimulating hormone, fT3= triiodothyronine
fT4= thyroxine

Table 5: Comparison of Thyroid function tests between HTN patients and Control

	HTN	Healthy control	
	Mean ± S. D	Mean ± S. D	P value
TSH	1.78 ± 1.30	2.84 ± 1.28	0.001*
fT4	13.47 ± 2.35	11.17 ± 1.93	0.000*
fT3	2.40 ± 0.47	2.37 ± 0.17	0.744

*=significant
TSH= Thyroid stimulating hormone, fT3= triiodothyronine
fT4= thyroxine

Pattern of Thyroid Dysfunction Profile in Patients and Controls

Table 6 further shows the distribution of thyroid dysfunction differences among the three groups. This showed that there was a 6.38%, 6.98% and 6.67% prevalence of dysfunction among the diabetics, hypertensives and control groups respectively.

Table 6: Pattern of thyroid dysfunction profile among diabetic patients, hypertensive patients and healthy control

	DM		**HTN**		**Control**		**Total**	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Euthyroid	44	93.62%	40	93.02%	28	93.33%	112	93.33%
Sick Euthyroid	1	2.13%	2	4.65%	2	6.67%	5	4.17 %
Subclinical Hypothyroidism	2	4.25%	1	2.33%	0	0	3	2.50 %
Clinical Hypothyroidism	0	0	0	0	0	0	0	0
Secondary Hypothyroidism	0	0	0	0	0	0	0	0
Subclinical Hyperthyroidism	0	0	0	0	0	0	0	0
Clinical Hyperthyroidism	0	0	0	0	0	0	0	0
Secondary Hyperthyroidism	0	0	0	0	0	0	0	0
Grand Total	47	100 %	43	100 %	30	100%	120	100 %

*The overall Prevalence of thyroid Dysfunction in Diabetic and Hypertensive patients is 6.38% and 6.98% respectively.

DISCUSSION

Diabetes mellitus is a major problem worldwide and despite advances in treatment a large number of patients present with complications due to poor glycaemic control. One of the possible factors that could contribute to poor glycaemic control is thyroid dysfunction, which tends to occur concomitantly with diabetes mellitus (Ogbonna and Ezeani, 2019). This study sought to find out the prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus.

The mean age of diabetic participants was 54 years, which typifies its prevalence in older adults. This is in line with widespread notions that advanced age can be a factor, as confirmed by Nwafor and Owhoji (2010) who found a mean age of 60.1 years in Port Harcourt, Nigeria, Celani *et al.* (1994), who found a mean age of 60 years old in Italy, and Papazafiroupoulou *et al.* (2010) who noted the mean age of diabetic to be around 65 years in Greece.

The prevalence rate of thyroid dysfunction (6.38%) in diabetics is remarkably close to the result of a population survey by Canaris *et al.* (2000) which revealed a prevalence of 6.6%, with prevalence significantly increased in the elderly. This may be explained by the fact that aging typically leads to development of organ specific and non-organ specific antibodies, hence higher prevalence of autoimmune thyroid dysfunction (Gesing, 2015).

Majority of the diabetic respondents with thyroid derangement presented with subclinical hypothyroidism (4.25%), and 2.13% were filed under Sick Euthyroid. This is lower than the findings of Uppal *et al.* (2013) who reported a 24.5% prevalence of thyroid dysfunction in diabetic patients. Akbar *et al.* (2006), in their study of 100 type 2 diabetics, also found that the prevalence of thyroid dysfunction was 16% and in control group of nondiabetics, it was 7%. Another possible reason is the difference in sample size by each study.

However, the results conformed to what the findings of Johnson (2006), Celani *et al.* (1994), Radaideh *et al.* (2004), and Rama *et al*. (2003), all of whom reported subclinical hypothyroidism as the most prevalent thyroid dysfunction. Khurana *et al.,* (2016) also reported that subclinical hypothyroidism was the most prevalent disorder in diabetic patients in their study, occurring in 7.5% of the test subjects, followed by hypothyroidism in 4.5%, hyperthyroidism in 2.5%, and subclinical hyperthyroidism in 1.5% of total 200 diabetic patients used as their test subject. This finding is also in agreement with the findings of Talwalkar *et al.* (2019), who reported a high prevalence of hypothyroidism in patients with type 2 diabetes. This study also supports their assertion and lends support to the existing literature in reporting the comorbidities among type 2 diabetics and hypothyroidism, and postulated that the higher prevalence of hypothyroidism could be attributed to higher mean glycemic status (HbA1c = 8.5%) within the cohort.

The significant difference in mean thyroid hormone levels between diabetics and the control group could be due to fact that in euthyroid individuals with diabetes, the serum T3 levels, basal TSH levels and TSH response to thyrotropin-releasing hormone (TRH) may all be strongly influenced by the glycemic status. Poorly-controlled diabetes may also result in impaired TSH response to TRH or loss of normal nocturnal TSH peak. The difference may also be due to the fact that the mean age of the diabetic group was significantly higher than the control group.

With respect to hypertensives, sick euthyroid respondents accounted for the larger share of patients with thyroid dysfunction with overall prevalence of thyroid dysfunction at 6.98%, which represents a lower prevalence than that reported by Papazafiropoulou *et al.* (2010) in Greece, as 85%. It is also in conflict with the 57.1% figure produced by a study by Sreelatha *et al.* (2017). However, the aforementioned study only used 14 hypertensives as subjects. So, selection bias and random bias may have played a large role in the high prevalence produced.

When comparing the mean thyroid function results, hypertensives posted a significant difference compared to the control group. This finding is in disagreement with Chubb *et al.* (2005) who found no independent association of altered thyroid profile with a history of systemic hypertension. However, the advanced average age of the hypertensive respondents may have been responsible for this disparity.

CONCLUSION

This represent a significant difference in fT4 levels between the diabetic and control group, and a significant difference in fT4 and TSH levels between the hypertensive group and control group. The prevalence of thyroid dysfunction was higher in Diabetics and Hypertensives than in the Apparently Healthy population, with more females affected than males. Subclinical hypothyroidism was found to be the commonest thyroid dysfunction in diabetics (4.25%) here in Kano, while sick Euthyroid was more common in Hypertensives (4.65%).

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