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Original Research

Pattern of Dysglycemia in Patients with Thyroid Disorders: A Tertiary Institution's Experience

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Abstract

Background: Thyroid hormone plays an integral role in glucose metabolism. It affects glucose homeostasis by impacting on the pancreatic β-cell function hence glucose metabolism. This study therefore aims to determine the pattern of dysglycemia in patients with thyroid disorders attending the endocrine clinic of the Lagos State University Teaching Hospital. **Methodology:** A retrospective study on all thyroid patients presenting at Endocrine Clinic of the Lagos State University Teaching Hospital (LASUTH) from January 2021 to May 2022. The results were presented as descriptive data and continuous variables. **Results:** About 46 patients' data were incomplete due to poor record keeping and retrospective nature of the study. One hundred patients had complete data which was analyzed. Hyperthyroidism accounted for 66% of thyroid disorders in our Endocrine clinic while hypothyroidism accounted for 21%. Dysglycemia was found in 22.7% cases of hyperthyroidism compared to 14% of patient with hypothyroidism. **Conclusion:** Dysglycemia is common in patients with thyroid disorder. Since thyroid disorder is a secondary cause of diabetes mellitus, we recommend early diagnosis and treatment of thyroid disorders.

Keywords: Dysglycemia, hyperthyroidism, thyroid disorder

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Introduction:

Thyroid hormone plays an integral role in glucose metabolism.[1-3] The thyroid hormone receptors are found in many tissues of the body including those responsible for glucose homeostasis such as liver, gastrointestinal tract, pancreas, adipose tissues, skeletal tissues and central nervous system. These tissues serve as sites for glycogenolysis, glycogenesis, lipolysis and gluconeogenesis. Glucose metabolism and homeostasis are regulated from interplay of many hormones which control mainly the process of glycogenolysis and gluconeogenesis.[4-5] These hormones are insulin, glucagon, cortisol and thyroid hormones. Other hormones involved are amylin, Glucagon Like Peptide 1 (GLP-1), growth hormone and epinephrine.[4-5]

The prevalence of thyroid disorder in Nigeria is 2.4% while in Africa it ranges between 1.2% and 9.9% .[6-8]The pattern of thyroid disorder showed hyperthyroidism accounted for 17.8% to 58% while hypothyroidism in 11.2% to 72% and euthyroid in 3.9% to 81.2% in these patients.[6-8]

Thyroid disorders and diabetes mellitus are associated with each other.[9,10] Autoimmunity is important in the relationship between dysglycemia and autoimmune thyroid disorder. Thyroid dysfunction which can manifest either as hyperthyroidism and hypothyroidism, is associated with insulin resistance and dysglycemia.[9,10]

Several studies have shown association between thyroid hormone and pancreatic β-cell function.[1-5]The pancreatic β-cells have thyroid hormone receptors (THRs) at birth. Specifically, triiodothyronine (T3) stimulates β-cell proliferation from birth through the first few weeks of life.[1-5] In addition, T3 increases glucose-stimulated insulin secretion in vivo.

Thyroid hormone control insulin secretion and glucose uptake and enhances glucose absorption by increasing gastrointestinal motility.[1-4] In liver, the thyroid hormones increases hepatic expression of glucose transporter 2 (GLUT2) responsible for endogenous production of glucose with resultant increase in gluconeogenesis and glycogenolysis.[1-5] Furthermore, stimulated glycogenolysis and gluconeogenesis results in hyperinsulinemia and glucose intolerance, resulting in peripheral insulin resistance. In the adipose tissue, it increases lipolysis resulting in an increase in free fatty acid which stimulates hepatic gluconeogenesis. Thyroid hormone also directly stimulates insulin secretion by pancreatic β-cells and increases glucagon release by pancreatic α-cells. Hyperthyroidism increases glucose transporter type 4 (GLUT4) gene expressions and glucose uptake in skeletal muscles.[1-5]

Some studies have demonstrated a higher prevalence of thyroid dysfunction in both type 1 and type 2 diabetes mellitus.[13,14] One of such studies reported a prevalence of 13.4% of thyroid disorders in people living with diabetes mellitus.[13,14] The prevalence was 31.4% in T1DM and 6.9% in T2DM. Sex prevalence showed 8.8% and 16.8% in men and women respectively.[10] Another meta-analysis in people living with diabetes mellitus revealed 11% prevalence of thyroid diseases.[11]Similar study in a Danish population as shown that hyperthyroid individuals were 43% more likely to be diagnosed with DM.[15,16] In a separate observational cohort study, hypothyroidism was linked to a 40% higher prevalence of DM compared to controls.[15,17]

There are few reported studies on the association between thyroid disorders on glucose metabolism in Nigeria as majority of the studies available were on prevalence and patterns of thyroid disorders .[6,7] This study aims to report the prevalence and pattern of dysglycemia in patient with thyroid disorders. Dysglycemia has been associated with increased cardiovascular morbidity hence the result of this study would assist clinicians in proper management and evaluation of thyroid disorders patients and reduce complications.

Study design and site
The study was a retrospective study carried out at the Lagos State University Teaching Hospital (LASUTH), Lagos, Nigeria. Lagos State University Teaching Hospital is located at Ikeja local government area of Lagos State in the South Western Nigeria.

Ethical approval
Ethical approval was obtained from Health Research and Ethics Committee of the Lagos State University Teaching Hospital (LASUTH), Lagos, Nigeria with reference number LREC/06/10/1980

Study Population
The population were patients seen at the Endocrine clinic of the Lagos State University Teaching Hospital (LASUTH) with endocrine related diseases from January 2021 to May 2022. One hundred and forty-six patients with thyroid disorders data were retrieved from the endocrine clinic records over the period of study

Eligibility criteria and sample size determination
The inclusion criteria were patient presenting with thyroid disorders attending the Endocrine clinic of Lagos State University Teaching hospital within the study period. The exclusion criteria were patient with previous diagnosis of diabetes mellitus.

Data collection and study procedure
The study was a retrospective study over seventeen months period (January 2021 to May 2022). This study was conducted at the out-patient Endocrinology clinic of the LASUTH. A convenient sampling method was employed and all consecutive patients with thyroid abnormalities were recruited into the study by retrieval of their case notes.
Clinical and sociodemographic data was documented using a study questionnaire including their thyroid function test, glucose readings, glycated hemoglobin, thyroid autoantibodies among others.

Data analysis
Data generated were analyzed using statistical package for social science (SPSS) version 26.Qualitative data were presented as count, percentages and graphs where appropriate. Quantitative data were presented as mean and standard deviation.

Result:
About 46 patients' data were incomplete due to poor record keeping and retrospective nature of the study. One hundred patients had complete data.

The mean age at presentation was 45.80±15.1 years with patients less than 40 years accounting for almost 50% of study population. About 68% of the patients had goiter while 96% had no family history of thyroid disorders. More females presented with thyroid disorders compared to the males. About 42% of the patient had normal body mass index, while 26% were obese. The mean weight was 26.54 ±5.3. See table 1

Table 1: Demographic pattern of patients who presented at the Endocrine clinic with thyroid disorders.

Variable	Frequency (n=100)	Percentage
Gender		
Male	10	10.0
Female	90	90.0
Age group (Years)		
≤40	46	46.0
41-60	39	85.0
>60	15	15.0
Mean±SD	45.80±15.1	
Marital status		
Single	19	19.0
Married	76	76.0
Others	5	5.0
Presence of Goiter		
Yes	68	68.0
No	32	32.0
Known Family history of thyroid disease		
Yes	4	4.0
No	96	96.0
Hypertensive status		
Present	27	27.0
Absent	73	73.0
Year since thyroid disorder diagnosis (Months)		
≤12	28	28.0
12-60	51	51.0

>60	21	21.0
Mean±SD	23.14±9.3	
BMI		
Underweight	3	3.0
Normal	42	42.0
Overweight	26	26.0
Obese	29	29.0
Mean±SD	26.54±5.3	

Hyperthyroidism accounted for over 66% of total thyroid disorder recorded while hypothyroidism accounted for 21% with others such as subclinical hypothyroidism and subclinical hyperthyroidism accounting for the remaining 13%. There was no record of Hashimoto thyroiditis (See figure 1).

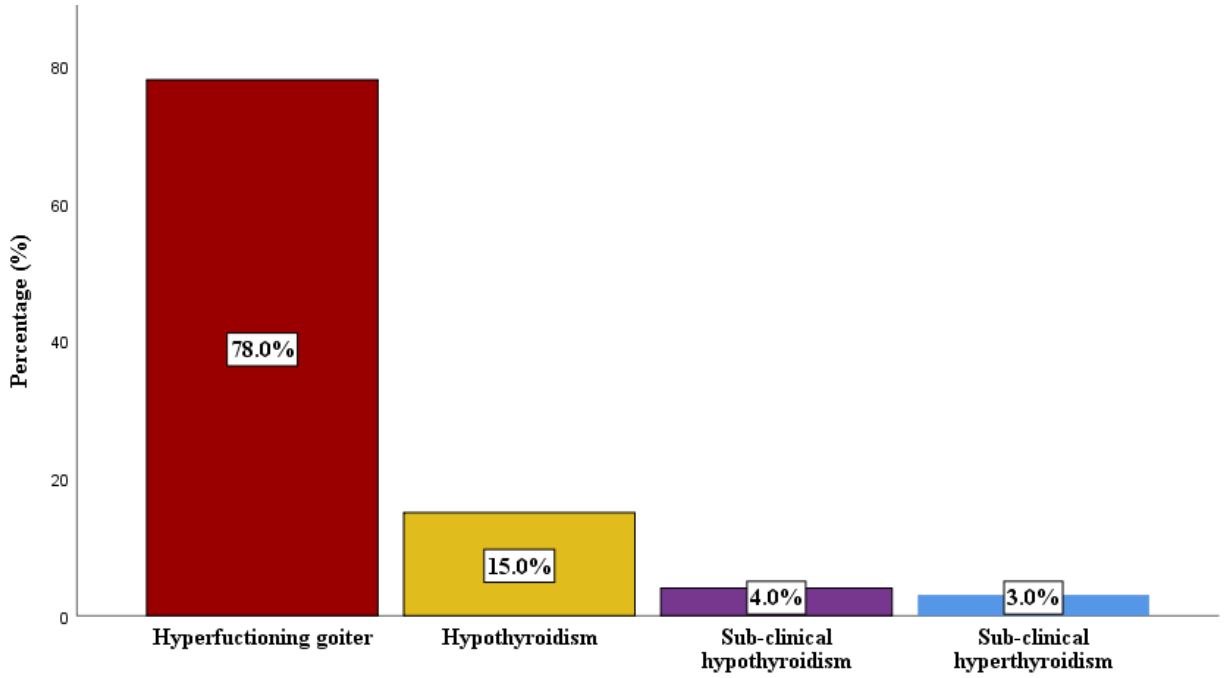

Figure 1. Types of thyroid disorder cases presented at the Endocrine clinic of LASUTH.

Figure 2 showed that autoimmune thyroid disorder accounted for 48.7% of the total cases of hyperthyroidism while 51.3% accounted for other causes of hyperthyroidism.

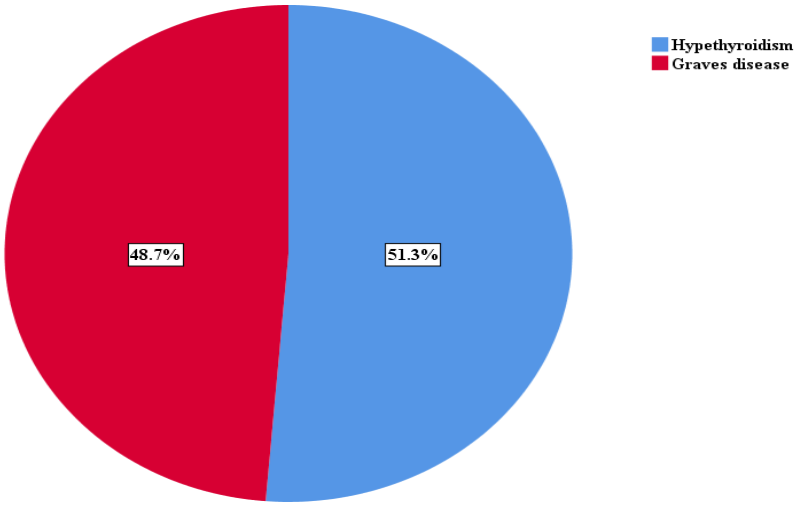

Figure 2 Autoimmune and non-autoimmune causes of hyperthyroidism presented at the Endocrine clinic of LASUTH.

About 80% of patients with thyroid disorders had normal blood glucose reading while 10% had diabetes mellitus and 9% with prediabetes. Only 1% had hypoglycemia (see figure 3).

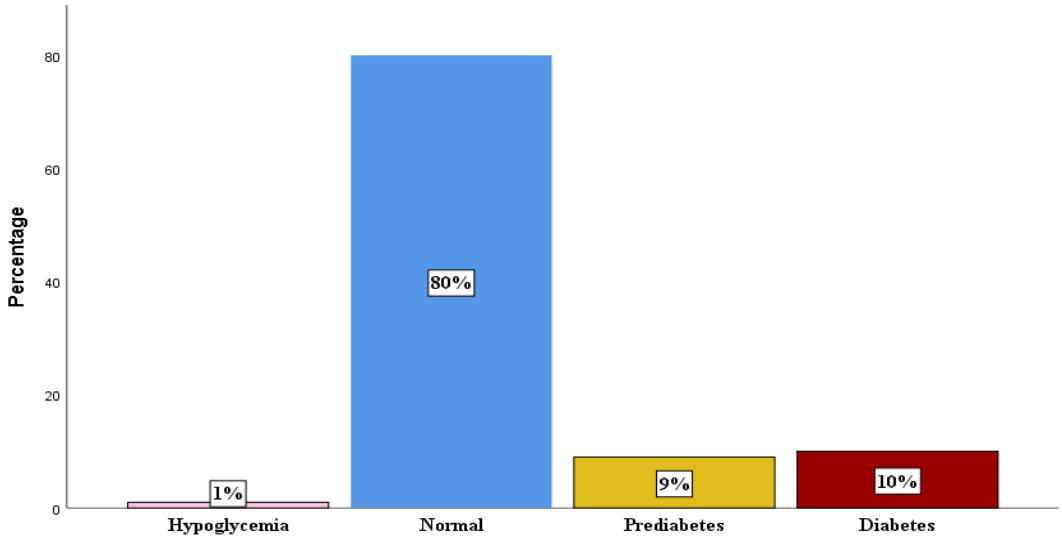

Figure 3. Pattern of dysglycemia in patients with thyroid disorder at the Endocrine clinic of LASUTH.

None of the patient with hyperthyroidism had hypoglycemia. The commonest dysglycemia in patients with hyperthyroidism was diabetes mellitus followed closely by prediabetes. Meanwhile patients with hypothyroidism had one recorded case of diabetes mellitus and hypoglycemia, others were euthyroid. Prior to diagnosis of thyroid dysfunction, none of the patients were diagnosed with dysglycemia. See table 2

Table 2: Association between dysglycemia and thyroid disorder

	Hypoglycemia	Normal	Prediabetes	Diabetes
Thyroid disorder				
Hyperfunctioning goitre	0(0.0)	61(76.2)	8(88.9)	9(90.0)
Hypothyroidism	1(100.0)	13(16.2)	0(0.0)	1(10.0)
Sub-clinical hypothyroidism	0(0.0)	3(3.8)	1(11.1)	0(0.0)
Sub-clinical hyperthyroidism	1(100.0)	3(3.8)	0(0.0)	0(0.0)

Dysglycemia was found in 22.7% cases of hyperthyroidism while it accounted for 14.3 % of patient with hypothyroidism. Those with dysglycemia had higher body mass index compared with those patients with normal glucose values (27.92 ± 6.3 versus 26.19 ±5.0 with p value 0.193). Also, those patients with dysglycemia were older compared to normoglycemia patients (47.40 ± 14.1 versus 43.95 ±14.9 with p value of 0.353). See table 3

Table 3: Association between dysglycemia and different thyroid disorders

	Dysglycemia	**Normal**	**χ^2**	**p-value**
Gender				
Male	**3(3.0)**	**7(70.0)**	**0.694**	**0.405**
Female	**17(18.9)**	**73(81.1)**		
Age (Years)	47.40±14.1	43.95±14.9	0.932*	0.353
BMI	27.92±6.3	26.19±5.0	1.310*	0.193
Year since thyroid disorder diagnosis (Months)	49.08±12.8	32.4±13.9	-1.269*	0.207
Presence of Goiter				
Yes	15(22.1)	53(77.9)	0.563	0.453
No	5(15.6)	27(84.4)		
Known Family history of thyroid disease				

Yes	1(50.0)	1(50.0)	0.065	0.799
No	19(19.4)	79(80.6)		
Hypertensive status				
Present	7(14.3)	42(85.7)	1.961	0.161
Absent	13(25.5)	38(74.5)		
Hyperthyroidism				
Present	15(22.7)	51(77.3)	0.902	0.342
Absent	5(14.7)	29(85.3)		
Hypothyroidism				
Present	3(14.3)	18(85.7)	0.542	0.461
Absent	17(21.5)	62(78.5)		
Sub-clinical hypothyroidism				
Present	1(9.1)	10(90.9)	0.919	0.338
Absent	19(21.3)	70(78.7)		
Sub-clinical hyperthyroidism				
Present	0(0.0)	3(100.0)	0.773	0.379
Absent	20(20.6)	77(79.4)		
Graves' disease				
Present	10(26.3)	28(73.7)	1.526	0.216
Absent	10(16.1)	52(83.9)		

*Independent student t test

Table 4 showed that patient with thyroid disorder who later developed diabetes mellitus had a higher BMI (28.36 ±6.6) compared with those who had hypoglycemia (23.50) with p value of 0.592

Table 4:Association between risk factors for dysglycemia and type of dysglycemia.

	Hypoglycemia	Prediabetes	Diabetes	**p-value**
Gender				
Male	0(0.0)	1(11.1)	2(20.0)	0.787
Female	1(100.0)	8(88.9)	8(80.0)	
Age (Years)	55.0	50.78±12.5	43.40±14.7	0.444

BMI	23.50±6.4	26.01±6.2	28.56±6.6	0.592
Year since thyroid disorder diagnosis (Months)	16.0	12.0 (12-24)	24.0 (12-108)	
Presence of Goiter				
Yes	1(100.0)	8(88.9)	8(80.0)	0.787
No	0(0.0)	1(11.1)	2(20.0)	
Known Family history of thyroid disease				
Yes	0(0.0)	0(0.0)	1(10.0)	0.591
No	1(100.0)	9(100.0)	9(90)	
Hypertensive status				
Present	1(100.0)	2(22.2)	1(10.0)	0.098
Absent	0(0.0)	7(77.8)	9(90.0)	

Discussion

Thyroid disorders and autoimmune disorders are commoner in young females.[17,18] This is similar to the findings in our study which showed that more females presented with thyroid disorders compared to the males with patients less than 40 years accounting for almost 50% of study population.

More patients had hyperthyroidism compared to other thyroid disorders accounting for about two thirds of the study population. Hyperthyroidism is the commonest thyroid disorder as demonstrated by Nyström HF et al and the incidence increases with age.[19] Ogbera et al demonstrated that the commonest thyroid disorder in Africa is hyperthyroidism.[7,8]Another similar study showed the most common thyroid disorder was hyperthyroidism with Graves disease accounting for the highest incidence.[20] In our study, Graves' disease accounted for almost 50% incidence of hyperthyroidism. Autoimmune thyroid disorder has some genetic predisposition with very low penetrance. In our study more than 90% had no family history of thyroid disorder.[20]

Dysglycemia was found in 22.7% cases of hyperthyroidism while it accounted for 14.3 % of patient with hypothyroidism. A study by Chang CH et al showed that patient with elevated serum thyroid-stimulating hormone concentration are at greater risk of developing prediabetes.[21] Similar study by Chaker L et al showed that low serum thyroid stimulating hormone even in the low-normal range as seen in subclinical hypothyroidism, increases the risk of diabetes by about 13%. [21]Patients who were prediabetes prior to subclinical hypothyroidism diagnosed have increased rate of progressing to diabetes mellitus.[22] Glucose metabolism is altered in both hypothyroidism and hyperthyroidism.

Hypothyroidism has resultant effect on glycemic control as it causes decreased glucose absorption, decreased hepatic glucose uptake, reduced liver gluconeogenesis and glycogenolysis with reduced muscle gluconeogenesis and glycogenolysis. There is associated insulin resistance in patients with subclinical and overt hypothyroidism. Hence hypothyroid patients are prone to both hypoglycemia and hyperglycemia.

Meanwhile, hyperthyroidism is associated with increased energy expenditure , increased appetite and caloric intake, increased lipolysis, and gluconeogenesis.[23]Thyroid hormone regulate insulin secretion and glucose uptake leading to enhanced glucose absorption by increasing gastrointestinal motility.[1-4] In liver, the thyroid hormones increases hepatic expression of glucose transporter 2 (GLUT2) responsible for endogenous production of glucose with resultant increase in gluconeogenesis and glycogenolysis.[1-5] In the adipose tissue, it increases lipolysis resulting in an increase in free fatty acid production which stimulates hepatic gluconeogenesis and increases insulin resistance.

Those with dysglycemia had higher body mass index compared with those patients with normal glucose values. Also, those patients with dysglycemia were older compared to normoglycemia patients. Overweight and obesity has been linked to onset of dysglycemia with increased cardiovascular morbidity and mortality.[24]

Patients with hyperthyroidism are more predisposed to the development of new onset diabetes mellitus or prediabetes compared with other thyroid disease. The findings in this study were similar to the study by Kalra S et al which showed thyrotoxicosis increases the risk of the new onset of diabetes mellitus and prediabetes.[25]Another study by Ray S. et al showed that 2-3% of euglycemic individuals with hyperthyroidism develop overt diabetes.[26]While about 50% of those with Graves' disease have some degree of glucose intolerance.[26] Those already living with Diabetic mellitus who developed hyperthyroidism experience worsened glycemic control. This is because thyrotoxicosis has been identified as a precipitant of hyperglycemic emergencies such as diabetic ketoacidosis.[27]

Conclusion

This study concluded that dysglycemia was common in patients with thyroid disease. Dysglycemia was more common in patients with hyperthyroidism than those with hypothyroidism. Patient with dysglycemia had higher body mass index and are older compared to those with normal blood glucose

Recommendations

Since thyroid disorder is a secondary cause of diabetes mellitus, we recommend early diagnosis and treatment of thyroid disorder to help in preventing complications associated with dysglycemia. Hence, dysglycemia should be routinely screened in patients with thyroid disorders to reduce the cardiovascular morbidity in these patients.

Areas of future research

There would also be need for larger and multicenter studies to look at the pattern of dysglycemia among patients with thyroid disorder which would enhance improved management of patient with thyroid disorder. Also, a larger prospective study would be needed to further establish the findings as the study was retrospective in nature.

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Nil

Conflicts of interest

There is no conflict of interest