

The Impact of Thyroid Dysfunction on Metabolism of Some Trace Elements in Subjects With Diabetes Mellitus in Edo South Senatorial District of Nigeria

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Abstract

Diabetes mellitus is characterized by impaired glucose metabolism and a resultant effect of persistent hyperglycaemia. Type 2 diabetes also known as adult-onset diabetes is majorly caused by insulin resistance. The objective of this study is to determine the effects of thyroid abnormality on anti-oxidative cofactors in subjects with diabetes mellitus in Edo South Senatorial district of Edo State. A total of 150 participants (100 subjects with diabetes mellitus and 50 apparently healthy individuals used as control) were recruited into this study. Thyroid function markers, Triiodothyronine and Thyroid stimulating hormone were analysed using chemiluminescence technique. While the trace elements; magnesium, zinc, selenium and copper were analysed using atomic absorption spectrophotometry. The data were analysed using statistical software for social science version 23 (IBM, Chicago IL, USA). For The thyroid hormones, there was a significant decrease in Triiodothyronine in diabetics as compared to the control group, with a non-significant increase in TSH. For the trace elements, only magnesium showed a significant decrease in the subject group when compared to the control group ($p=0.007$), with zinc, copper and selenium depicting no statistical significance. The relationship between thyroid hormones and trace elements showed no statistical significance. The correlation between thyroid hormones levels and selenium likewise showed no significant relationship statistically. This study revealed that accompanied by diabetes mellitus is the induction of hypothyroidism, characterized by significant decrease in Triiodothyronine and a non-significant increase in Thyroid Stimulating Hormone. Also discovered, was the significant

decrease in the levels of magnesium in diabetics as compared to their non-diabetic counterparts. Addressing these thyroid hormone derangements and hypomagnesemia in diabetes mellitus could help endocrinologists and other concerned healthcare providers in providing well-informed clinical intervention for sufferers.

Keywords: Diabetes Mellitus, Copper, Magnesium, Zinc, Selenium, Triiodothyronine(T3), Thyroid Stimulating Hormone (TSH).

Introduction

Diabetes mellitus is a metabolic disorder characterized by elevated blood glucose levels due to the body's inability to produce or effectively utilize insulin (*American Diabetes Association*, 2023). This chronic condition can lead to various complications, including dysthyroidism, inflammatory responses, and oxidative stress. Exploring the relationship between these factors and the role of anti-oxidative co-factors could be pivotal in the management of diabetes mellitus.

Dysthyroidism, which encompasses both hypothyroidism and hyperthyroidism, is a common comorbidity in individuals with diabetes mellitus. This association is bidirectional, with diabetes increasing the risk of thyroid dysfunction and vice versa. The underlying mechanisms behind this relationship are not fully understood, but it is believed to involve factors such as insulin resistance, oxidative stress, and autoimmune processes (Kalra and Sahay, 2022).

The coexistence of these conditions could worsen metabolic disturbances, leading to poor glycaemic control and an increased risk of complications (Kuo *et al.*, 2019). The underlying mechanisms involve alterations in insulin sensitivity, glucose metabolism, and thyroid hormone regulation (Kalra and Sahay, 2022).

Oxidative stress, characterized by an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defense mechanisms, plays a significant role in the pathogenesis of diabetes mellitus (Yaribeygi *et al.*, 2020). Hyperglycaemia is a hallmark of diabetes and promotes the formation of ROS, which can damage cellular components, including proteins, lipids, and DNA. This oxidative stress contributes to the development of various diabetic complications, such as neuropathy, nephropathy, and retinopathy. Hyperglycaemia and dyslipidaemia contribute to the increased production of ROS, which can damage cellular components, including lipids, proteins, and Deoxyribonucleic acid (DNA) (Newsholme *et al.*, 2016). Oxidative stress is also implicated in the development of diabetic complications, such as nephropathy, neuropathy, and retinopathy. To combat the detrimental effects of oxidative stress, the body relies on various antioxidant defense mechanisms, including enzymatic and non-enzymatic antioxidants (Newsholme *et al.*, 2016).

Anti-oxidative cofactors which include trace elements like zinc, copper, magnesium and selenium, play a vital role in counteracting oxidative stress and mitigating its deleterious effects. These cofactors act as scavengers of ROS, enhancing the body's antioxidant defense mechanisms and potentially reducing the risk of diabetic complications. However, the efficacy of antioxidant supplementation in managing diabetes mellitus remains a subject of ongoing research and debate (Asemi *et al.*, 2015).

These cofactors can help neutralize ROS, prevent oxidative damage, and potentially mitigate the progression of diabetic complications. Dysthyroidism and oxidative stress are closely intertwined with the pathophysiology of diabetes mellitus. Understanding these intricate relationships is crucial for developing effective

strategies to manage and prevent diabetic complications. The incorporation of anti-oxidative cofactors, in conjunction with appropriate medical interventions, may hold promise in mitigating the deleterious effects of oxidative stress and improving overall outcomes for individuals with diabetes mellitus.

Research Methodology

Study Area and Population

This study will be carried out at Edo Specialist Hospital, Benin City, Edo State. The study population for this research is diabetic patients attending the endocrinology clinic of Edo Specialist Hospital, Benin City, Edo State. Apparently healthy male and female subjects; with a normal glucose metabolism served as the control group. Therefore, a minimum of 100 test samples and 50 controls were used for this study.

Study Criteria

Adult male and female subjects with laboratory evidence of being diabetic, adult male and female subjects who gave an informed consent to participate in this study were included in the study. While adult male and female subjects with no evidence of impaired glucose metabolism, adult male and female subjects who refused to grant informed consent for participation were excluded from the study.

Sample Collection

About five millilitres of blood was collected aseptically from the cubital fossa of each subject by an experienced phlebotomist using an aseptic collection procedure as described by Cheesborough (2000), dispensed into plain sample container and allowed to clot. After clot retraction, samples are centrifuged, and the supernatant was collected into another plain container. Sample was then stored at freezing temperature until analysis.

Laboratory Analyses

Determination of Triiodothyronine Using Abbott Autoanalyser

Principle: Abbott Auto-analyser is an automated clinical chemistry analyzer used for the analysis of a wide range of biochemical markers in patient blood and serum samples. The principle of operation of the Abbott

Autoanalyzer is based on chemiluminescence. Activated ions get excited by absorbed energy and move from their respective ground states to higher energy levels. Upon return to their initially occupied ground state, these ions emit their absorbed energy.

Method: The patient's blood sample was prepared by centrifugation to separate the cells from the serum. The serum is then loaded onto the instrument.

The Abbott Auto-analyser uses pre-packaged reagent kits that contain all the necessary reagents for the analysis of specific biochemical markers. These reagents were loaded into the instrument, along with calibrators and quality control samples.

The instrument automatically dispenses a measured volume of the patient's sample into a reaction vessel containing the appropriate reagents. The reaction between the sample and the reagents produced a coloured compound, the intensity of which is proportional to the concentration of the analyte being measured.

The reaction vessel was placed into the instrument, which measures the absorbance of the coloured compound at a specific wavelength of light. The absorbance measurement is compared to a calibration curve generated using the calibrators, and the concentration of the analyte in the patient's sample was determined.

Quality control: The Abbott Auto-analyser also includes built-in quality control features to ensure the accuracy and precision of the analysis. These features include the use of quality control samples, automated calibration, and instrument maintenance checks.

Determination of "Thyroid Stimulating Hormone Using Abbott Autoanalyzer.

Principle: Abbott Auto-analyser is an automated clinical chemistry analyser used for the analysis of a wide range of biochemical markers in patient blood and serum samples. The principle of operation of the Abbott Auto-analyser is based on chemiluminescence. Activated ions get excited by absorbed energy and move from their

respective ground states to higher energy levels. Upon return to their initially occupied ground state, these ions emit their absorbed energy

Method: The patient's blood was prepared by centrifugation to separate the cells from the serum. The serum is then loaded onto the instrument.

The Abbott Auto-analyser uses pre-packaged reagent kits that contain all the necessary reagents for the analysis of specific biochemical markers. These reagents were loaded into the instrument, along with calibrators and quality control samples.

The instrument automatically dispenses a measured volume of the patient's sample into a reaction vessel containing the appropriate reagents. The reaction between the sample and the reagents produced a coloured compound, the intensity of which is proportional to the concentration of the analyte being measured.

The reaction vessel was placed into the instrument, which measures the absorbance of the coloured compound at a specific wavelength of light. The absorbance measurement is compared to a calibration curve generated using the calibrators, and the concentration of the analyte in the patient's sample was determined.

Quality control: The Abbott Auto-analyser also includes built-in quality control features to ensure the accuracy and precision of the analysis. These features include the use of quality control samples, automated calibration, and instrument maintenance checks.

Determination of Copper, Zinc, Selenium and Magnesium using Atomic Absorption Spectrophotometry

Principle: Atomic absorption spectrophotometry (AAS) is a commonly used analytical technique for the quantitative analysis of trace elements in a wide range of samples, including environmental, clinical, and biological specimens. The principle of the AAS method involves the measurement of the absorbance of light by free atoms in a gaseous state.

Method: The sample was prepared by acid digestion that convert the sample into a solution that can be aspirated into the AAS instrument. The solution containing the analyte was aspirated into a flame, usually a flame produced by burning acetylene and air, where the sample is vaporized and the atoms of the analyte was excited to higher energy levels. A beam of light, usually from a hollow cathode lamp that emits light at the specific wavelength corresponding to the element being analysed, was passed through the flame. The atoms of the analyte in the flame absorb some of the light, resulting in a decrease in the intensity of

the transmitted light. The amount of light absorbed by the analyte was measured by a detector, and the absorbance was converted to concentration using a calibration curve generated using standard solutions of known concentration.

Quality control: AAS instruments include built-in quality control features to ensure the accuracy and precision of the analysis. These features include the use of blank solutions, reference standards, and control samples.

Result

Table 1: Comparison of Thyroid Hormones Among Study Participants

Variables	Diabetics (Test) n=100	Non-Diabetics (Control) n=50	t-value	P-value
T3	2.7940±1.4328	3.8420±1.1337	4.056	0.000
TSH	12.2700±8.8267	12.0180±7.6752	-0.152	0.879

The result above show that for some thyroid hormones, there was a significant decrease ($P < 0.05$; $P = 0.00$) for the T3 of the diabetic groups when compared to the test groups and a non-significant increase in the TSH level of the diabetic group when compared to the test groups. This result shows that diabetes mellitus is characterized by dysregulation of thyroid hormones, as depicted by the ongoing hypothyroidism.

Table 2: Comparison of Anti-Oxidative Co-Factors Among Study Participants

Variables	Diabetics (Test)n=100	Non-Diabetics (Control)n=50	t-value	P-value
Copper	0.8126±0.2219	0.8626±0.1950	1.197	0.234
Magnesium	19.0702±3.3523	20.9584±3.5065	2.752	0.007
Zinc	1.2318±0.4492	1.1140±0.4055	-1.377	0.172
Selenium	0.0986±0.0357	0.1118±0.0377	1.796	0.076

Table 2 shows results for the anti-oxidative co-factors, only magnesium showed a significant ($P < 0.05$; $P = 0.007$) decrease for the diabetic group when compared to the non-diabetic group while Copper, Zinc and Selenium were not significant. This invariably implies that accompanied by impaired glucose metabolism as seen in diabetes mellitus is hypomagnesemia

Table 3: Correlation of Some Thyroid Hormones and Anti-Oxidative Co-Factors

Thyroid Hormones	Anti-Oxidative Stress markers	r-value	P-value	Remark
TSH	Copper	-0.364	0.009	NSNSC
	Zinc	-0.018	0.903	NWNSC
	Magnesium	0.084	0.560	PWNSC
	Selenium	0.035	0.808	PWNSC
T3	Copper	-0.006	0.966	NWNSC
	Zinc	-0.011	0.937	NWNSC
	Magnesium	-0.171	0.236	NWNSC
	Selenium	0.121	0.403	PWNSC

Key: *NWNSC*= Negative Weak Non- Significant Correlation, *PWNSC*= Positive Weak Non-Significant Correlation

Table 3 below shows the relationship between thyroid stimulating hormone, triiodothyronine, selenium and glutathione peroxidase, with no significant correlation established between these respective parameters.

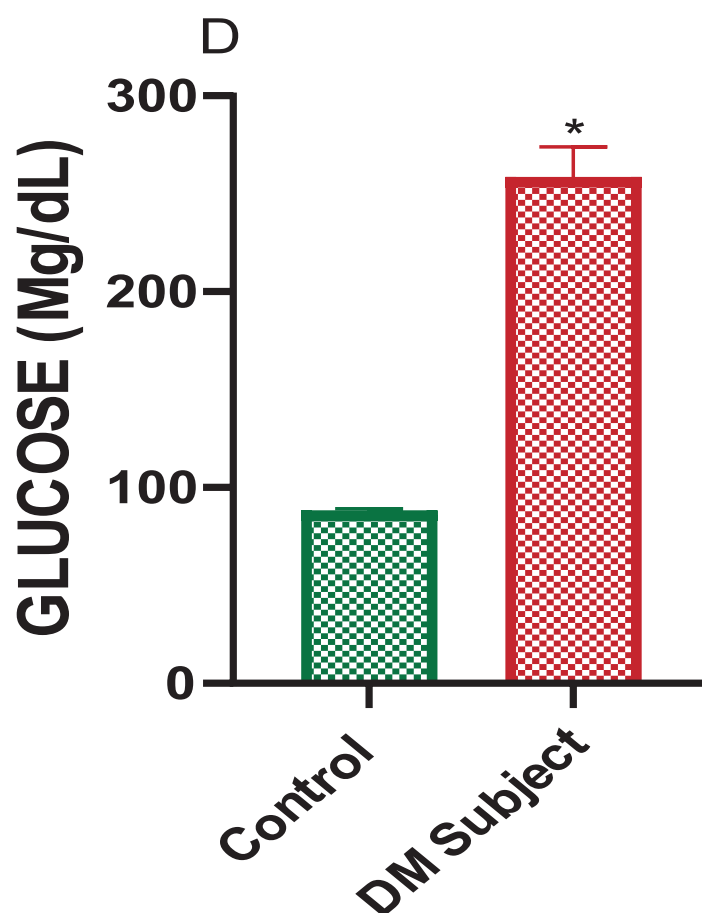


Figure 1: The Level of glucose in DM Subjects.

The values are given as Mean ± SEM of 100 replicates. Data were analysed by unpaired T-test (and nonparametric tests). *P<0.05 vs Control.

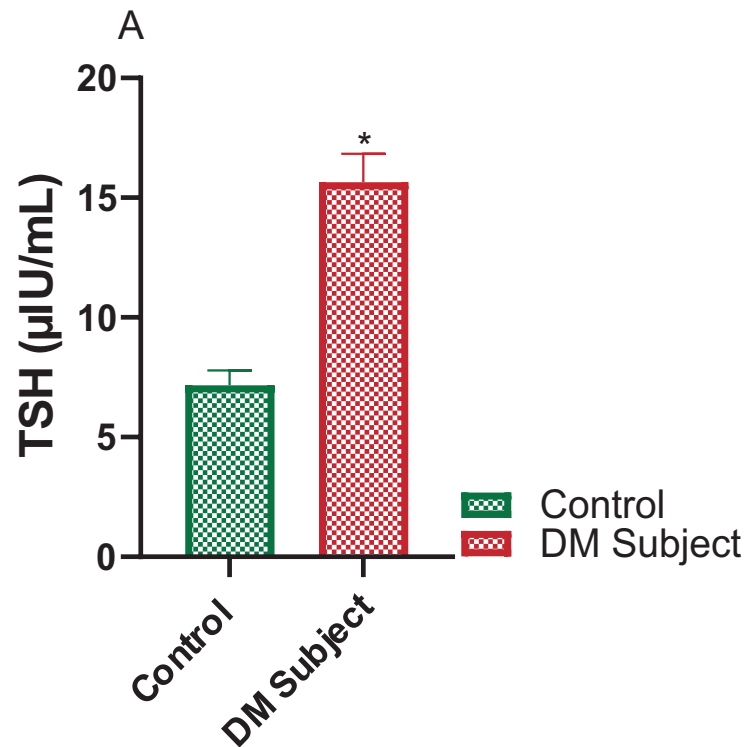


Figure 2: The Level of Thyroid hormones, thyroid stimulating hormone, TSH in DM Subjects. The values are given as Mean \pm SEM of 100 replicates. Data were analysed by unpaired T-test (and nonparametric tests). *P<0.05 vs Control.

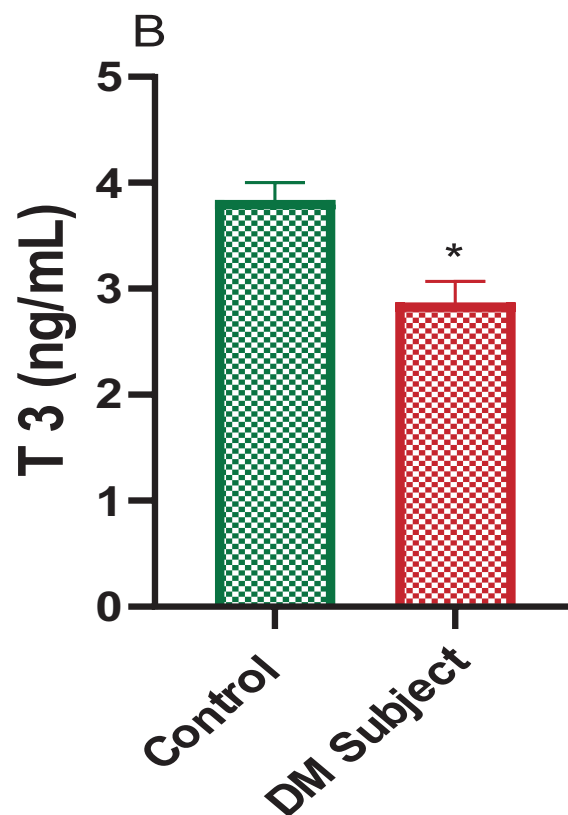


Figure 3: The Level of triiodothyronine, T3 (B) in DM Subjects. The values are given as Mean \pm SEM of 100 replicates. Data were analysed by unpaired T-test (and nonparametric tests). *P<0.05 vs Control.

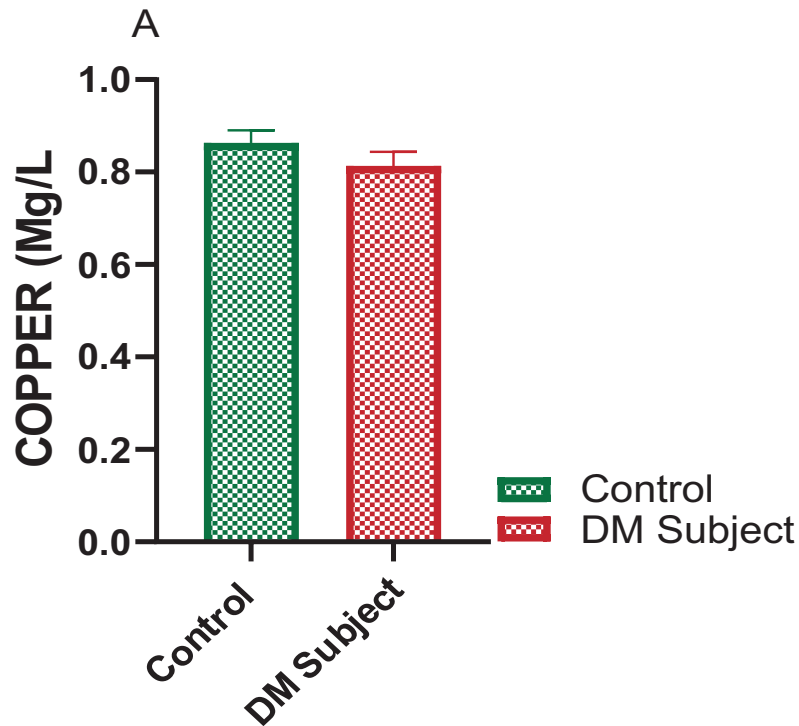


Figure 4: The Level of copper, Cu in DM Subjects.

The values are given as Mean \pm SEM of 100 replicates. Data were analysed by unpaired T-test (and nonparametric tests). *P<0.05 vs Control.

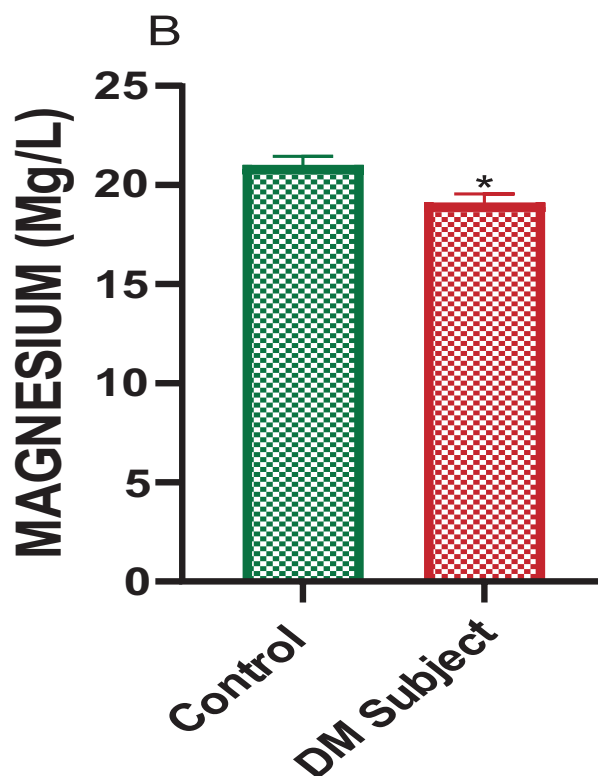


Figure 5: The Level of magnesium, Mg in DM Subjects.

The values are given as Mean \pm SEM of 100 replicates. Data were analysed by unpaired T-test (and nonparametric tests). *P<0.05 vs Control.

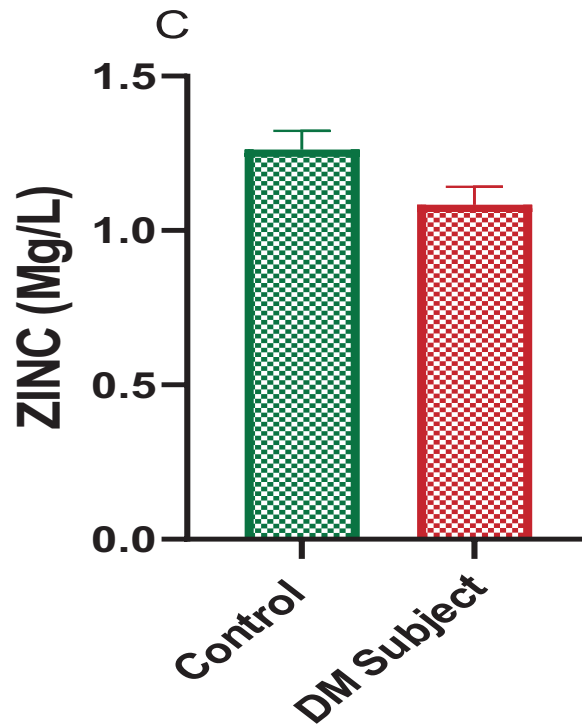


Figure 6: The Level of Zinc in DM Subjects.

The values are given as Mean \pm SEM of 100 replicates. Data were analysed by unpaired T-test (and nonparametric tests). *P<0.05 vs Control.

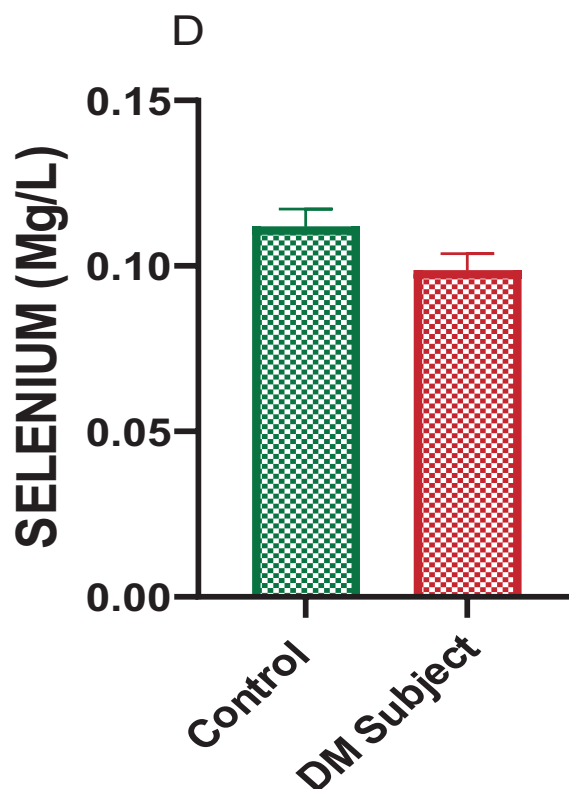


Figure 7: The Level of Selenium in DM Subjects.

The values are given as Mean \pm SEM of 100 replicates. Data were analysed by unpaired T-test (and nonparametric tests). *P<0.05 vs Control.

Discussion

Thyroid dysfunction refers to thyroid disorders, which can manifest either hyperthyroidism or hypothyroidism, commonly coexisting with metabolic conditions such as diabetes. Diabetes intensifies both inflammation and oxidative stress, primarily due to the heightened production of reactive oxygen species (ROS) stemming from glucose metabolism and impaired mitochondrial function. Continual high levels of blood sugar worsen the production of reactive oxygen species (ROS), leading to tissue damage and exacerbating complications, even though antioxidant defenses may become overwhelmed in diabetic individuals. The results presented in Table 2 demonstrate a significant increase in thyroid stimulating hormone (TSH) levels (as shown in Figure 2) in the diabetic group compared to the non-diabetic control group. Conversely, the levels of triiodothyronine (T3) (as depicted in Figure 3) showed a significant decrease in diabetic subjects compared to control subjects. In contrast to the results regarding thyroid stimulating hormone (TSH) in this study, the research conducted by Wolide *et al.* (2017) on the association between thyroid hormone parameters and dyslipidaemia among type 2 diabetes mellitus patients: Comparative cross-sectional study' reported a significant decrease in TSH levels among diabetic patients compared to the control (non-diabetic) group. The decrease in thyroid stimulating hormone (TSH) levels could result from changes in feedback mechanisms within the hypothalamic-pituitary-thyroid axis, influenced by factors like insulin resistance and glucose levels, which may suppress the secretion of TSH. The results of this study are consistent with those of Moura Neto *et al.* (2016), who also found a significant decrease in T3 levels among diabetic participants compared to controls. The notable decrease in T3 observed in this study may be linked to the medications administered to diabetic patients. For example, phenylthiourea may suppress levels of FT4 and T4, leading to elevated levels of TSH. Additionally, insulin administration may enhance levels of FT4 while suppressing T3 levels by inhibiting the hepatic conversion of T4 to T3. Subjects with diabetes mellitus demonstrated thyroid hormone imbalances such as hypothyroidism, which

reduces antioxidant enzyme activities primarily through its effects on gene expression and enzyme synthesis leading to decreased protection against oxidative stress. This phenomenon likely occurred due to either enhanced glycosylation and platelet aggregation or impairment of cellular antioxidant protective systems. The heightened production of free radicals may contribute to the development of metabolic vasculopathy. The result for T3 demonstrated a significant decrease in diabetic subjects compared to the control group. The results regarding T3 in this study oppose those of Fei *et al.* (2018), who found in their study on "Thyroid stimulating hormone and free triiodothyronine are valuable predictors for diabetic nephropathy in patients with type 2 diabetes mellitus" that there was no significant difference in T3 levels between controls and patients without complications ($p > 0.05$). In contrast, patients with diabetic nephropathy demonstrated decreased levels of triiodothyronine (T3). The decrease in T3 levels among diabetic patients may result from changes in the peripheral conversion of thyroxine (T4) to T3, influenced by factors like insulin resistance and impaired glucose metabolism. This leads to a reduction in thyroid hormone synthesis and availability. In subjects with diabetes mellitus, thyroid hormones can influence metabolism and utilization of trace elements such as selenium, zinc, and copper primarily through their effects on metabolism and transport mechanisms. For example, thyroid hormones regulate the expression of transport proteins involved in the uptake and distribution of trace elements such as selenium, zinc, and copper. The results presented in Table 3 demonstrated the relationship between thyroid hormones and trace elements in diabetic mellitus patients. The findings reveal a significant increase in thyroid stimulating hormone (TSH). The results regarding thyroid stimulating hormone (TSH) in this study are consistent with those of Wolide *et al.* (2017) in their study on "Association between thyroid hormone parameters and dyslipidemia among type 2 diabetes mellitus patients: Comparative cross-sectional study." Their findings also reported a significant increase in TSH levels among diabetic patients compared to the control (non-diabetic) group. These changes could stem

from insulin resistance and hyperglycemia, potentially interfering with the feedback loop of the hypothalamic-pituitary-thyroid axis. In this study, both T3 and magnesium exhibited significant decrease in diabetic subjects compared to control subjects. The results of this study are consistent with those of Moura Neto *et al.* (2016), which demonstrated a notable decrease in T3 levels among study participants (the diabetic group) compared to controls. Additionally, Barbagallo and Dominguez (2015) noted a decline in serum magnesium levels correlated with increase in HbA1c levels and the duration of Type 2 Diabetes Mellitus, which corresponds with the findings of this study. Decreased T3 levels in diabetic patients could be attributed to medication usage that interferes with the conversion of T4 to T3. Likewise, the decrease in magnesium levels could be a consequence of heightened urinary excretion triggered by hyperglycaemia. The correlation coefficients (r) between serum selenium and serum TSH levels in diabetic mellitus patients indicate a weak inverse relationship, suggesting a potential impact of selenium on thyroid function, as depicted in Table 3. However, the results do not reveal any significant ($p < 0.05$) correlation coefficients (r) between selenium, TSH, and T3. The mentioned results contrast with those of Kobayashi *et al.* (2021), whose study observed a 14% increase in TSH and a noteworthy decrease in T3 levels among 22 subjects with selenium deficiency. Additionally, a study conducted by Narayana *et al.* (2014), noted a notable decline in serum selenium and T3 levels in diabetic subjects compared to controls. This phenomenon could potentially be attributed to selenium's involvement in thyroid hormone synthesis and metabolism. Studies have shown that in diabetic mellitus patients, trace elements like selenium, zinc, and copper play crucial roles in modulating redox parameters such as antioxidant enzyme activities and oxidative stress levels. Alterations in trace element status can disrupt the balance between oxidant and antioxidant defenses, contributing to increased oxidative stress and tissue damage observed in diabetes. Conversely, supplementation or optimization of trace element levels may help restore redox balance and mitigate

complications associated with diabetes. Based on the results of this study, as depicted in Table 2, diabetic subjects exhibited a significant decrease in magnesium compared to control subjects. The results of this study regarding magnesium levels are consistent with those of Arpaci *et al.* (2017), whose research on "Associations of serum Magnesium levels with diabetes mellitus and diabetic complications" identified a significant magnesium depletion. They suggest that hyperinsulinemia-related urinary magnesium excretion, insufficient nutrition, and possibly a particular renal defect might contribute to this occurrence. Regarding thyroid functions, the study conducted by De Vries *et al.* (2019), found no apparent correlation between plasma TSH levels within the normal range and Type 2 diabetes mellitus, which contradicts the findings of this study. A separate study by Ogbonna *et al.* (2019), noted a significant decrease in T3 levels, a result that is consistent with the findings of this study. The changes in thyroid function seen in diabetic patients could stem from the impact of hyperglycemia on thyroid hormone metabolism or autoimmune thyroid diseases, resulting in fluctuations in thyroid hormone levels compared to non-diabetic individuals.

Conclusion

Individuals with diabetes mellitus exhibit dysthyroidism, marked by significant decrease in T3 and non-significant decrease in TSH. This was accompanied by a significant decrease in magnesium level. It has also been established that there is hypomagnesemia in subjects with diabetes mellitus, with no significant effect on copper, zinc and selenium. These findings underscore the intricate interplay between dysglycaemia, thyroid dysfunction and anti-oxidative cofactors in the pathophysiology of diabetes mellitus. Understanding these relationships may inform targeted therapeutic interventions to mitigate the complications associated with diabetes mellitus.

Recommendation

Based on the findings regarding dysthyroidism, inflammatory response, oxidative stress, and antioxidative stress levels in subjects with diabetes mellitus, several recommendations can be made:

1. Health care providers should implement routine thyroid function tests in diabetic patients to detect and manage dysthyroidism early, thus reducing the risk of complications.
2. Magnesium levels of diabetic patients should be routinely analyzed and derangement should be commensurately managed using necessary diets and/or supplementation.

Contribution to Knowledge

1. The study highlights specific biomarkers, including TSH, glucose, T3, and magnesium, that exhibit significant alterations in subjects with diabetes mellitus. This identification of biomarkers provides valuable insight into dysthyroidism, and oxidative stress in diabetic individuals.
2. By demonstrating significant increase in TSH and glucose, as well as significant decrease in T3, and magnesium, the study contributes to the concomitant presence of dysthyroidism, and hypomagnesemia in diabetes mellitus.
3. The observed alterations in TSH, T3, and magnesium levels may serve as potential biomarkers for risk stratification in diabetic individuals. Monitoring these biomarkers could aid in identifying patients at higher risk of developing complications associated with hyperglycaemia, thyroid dysfunction and oxidative stress.
4. The study highlights potential therapeutic targets for managing diabetes mellitus and its complications. Interventions aimed at correcting hypothyroidism, enhancing antioxidant enzyme activity, and optimizing magnesium levels could be explored to mitigate the adverse effects of thyroid dysfunction, and oxidative stress in diabetic patients.

LIST OF ABBREVIATIONS

ELISA: Enzyme Linked Immuno-sorbent Assay

T3: Triiodothyronine

TSH: Thyroid Stimulating Hormone

AGES: Advanced Glycation End Products

ROS: Reactive Oxygen Species

T2DM: Type 2 Diabetes Mellitus

HBA1C: Haemoglobin A1C

AAS: Atomic Absorption Spectrophotometry

Ethical Approval and Consent to Participate

The approval for this study was given by the ethical committee of Health Research Ethics Committee of Edo State Ministry of Health, Benin City, Edo State, Nigeria. Informed consent was obtained from each participant prior to specimen collection.

Availability of Data and Materials

The authors declare consent for all available data present in this study.

Author's Contributions

Conception and design of the work/idea: Christian Onosetale Ugege and Mathew Folaranmi Olaniyan

Collect data/obtaining results: Christian Onosetale Ugege

Manuscript writing: Christian Onosetale Ugege
Analysis and interpretation of data: David Olufemi Adebo and Odekunle Bola Odegbemi

Critical revision of the manuscript: Teddy Ilenagbe, Edward Eghonghon Imadojemu and Ekomobong Effiong Idem

Final research review: Mathew Folaranmi Olaniyan

Competing Interests

The authors declare no conflicts of interest

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References

- American Diabetes Association (2023). Standards of medical care in diabetes—2023. *Diabetes Care*; **46(1)**:1-229.
- Acharya, A.B., Thakur, S., Muddapur, M.V. (2015). Evaluation of serum interleukin-10 levels as a predictor of glycemic alteration in chronic periodontitis and type 2 diabetes mellitus. *Journal of Indian Society of Periodontology*; **19(4)**: 388-392.
- Animaw, W., Seyoum, Y. (2017). Increasing prevalence of diabetes mellitus in a developing country and its related factors. *PloS One*; **12(11)**: 187670.
- Arpaci, D., Tocoglu, A.G., Ergenc, H., Korkmaz, S., Ucar, A., Tamer, A. (2015). Associations of serum Magnesium levels with diabetes mellitus and diabetic complications. *Hippokratia*; **19(2)**: 153.
- Asemi, Z., Karamali, M., Esmailzadeh, A. (2015). Effects of calcium-vitamin D co-supplementation on glycaemic control, inflammation and oxidative stress in gestational diabetes: A randomised placebo-controlled trial. *Diabetologia*; **58(9)**: 1919-1928.
- Barbagallo, M., and Dominguez, L.J. (2015). Magnesium and type 2 diabetes. *World Journal of Diabetes*; **6(10)**:152-1157.
- Cheesbrough, M. (2000). District Laboratory Practice Manual in Tropical Countries. Cambridge University Press, Cambridge:178-179.
- De Vries, T. Kappelle, L.J., van der Graaf, Y., de Valk, H.W., de Borst, G.J., Nathoe, H.M., Visseren, F.L.J., Westerink, J., SMART study group. (2019). Thyroid-stimulating hormone levels in the normal range and incident type 2 diabetes mellitus. *Acta diabetologica*; **56**: 431-440.
- Esser, N., Legrand-Poels, S., Piette, J., Scheen, A.J., Paquot, N. (2014). Inflammation as a link between obesity, metabolic syndrome and type 2 diabetes. *Diabetes Research and Clinical Practice*; **105(2)**: 141-150.
- Fei, X., Xing, M., Wo, M., Wang, H., Yuan, W., Huang, Q. (2018). Thyroid stimulating hormone and free triiodothyronine are valuable predictors for diabetic nephropathy in patient with type 2 diabetes mellitus. *Annals of Translational Medicine*; **6(15)**: 305. doi: 10.21037/atm.2018.07.07.
- Kalra, S., and Sahay, R. (2022). Diabetes and thyroid disorders. *Journal of the Pakistan Medical Association*; **72(4)**: 813-817.
- Kuo, I.C., Sah, S.K., Kc, R., Baral, N., Lamsal, M. (2019). Thyroid dysfunction in diabetic patients with metabolic syndrome. *The Journal of Endocrinology and Metabolism*; **9(1-2)**: 22-29.
- Liamis, G., Liberopoulos, E., Barkas, F., Elisaf, M. Diabetes mellitus and electrolyte disorders. *World Journal of Clinical Cases*; **2(10)**: 488-496. doi: 10.12998/wjcc.v2.i10.488.
- Mishra, S. and Mishra, B.B. (2017). Study of lipid peroxidation, nitric oxide end product, and trace element status in type 2 diabetes mellitus with and without complications. *International Journal of Applied and Basic Medical Research*; **7(2)**: 88-93.
- Moura Neto, A., Parisi, M.C., Alegre, S.M., Pavin, E.J., Tambascia, M.A., Zantut-Wittmann, D.E. (2016). Relation of thyroid hormone abnormalities with subclinical inflammatory activity in patients with type 1 and type 2 diabetes mellitus. *Endocrine*; **51**: 63-71.
- Narayana, K., Uchuru, A., Basha, S., Shaker, I.A. (2014). The evaluation of selenium and thyroid hormones among the population with diabetes mellitus. *Indian Journal of Basic and Applied Medical Research*; **1**: 251-258.
- Naz, S., Shafique, N., Sharif, S., Manzoor, F., Safi, S. Z., Firasat, S., & Kaul, H. (2020). Association of interleukin 10 (IL-10) gene with type 2 diabetes mellitus by single nucleotide polymorphism of its promoter region G/A 1082. *Critical Reviews in Eukaryotic Gene Expression*. **30(4)**: :285-289. doi: 10.1615/CritRevEukaryotGeneExpr.2020030714.
- Newsholme, P., Cruzat, V., Arfuso, F., Keane, K. (2016). Nutrient regulation of insulin secretion and action. *The Journal of Endocrinology*; **231(1)**:105-120.
- Ogbonna, S.U., Ezeani, I.U., Okafor, C.I.,

- Chinenye, S. (2019). Association between glycemic status and thyroid dysfunction in patients with type 2 diabetes mellitus. *Diabetes, metabolic syndrome and obesity: Targets and Therapy*:1113-1122.
- Qin, K., Zhang, F., Wu, Q., Liu, Z., Huang, Y., Tan, J., Zhou, Y., An, Z., Li, S., Li. S. (2020). Thyroid hormone changes in euthyroid patients with diabetes. *Diabetes, Metabolic Syndrome and Obesity*; **13**: 2533-2540.
- Wolide, A.D., Zawdie, B., Alemayehu, T., Tadesse, S. (2017). Association between thyroid hormone parameters and dyslipidemia among type 2 diabetes mellitus patients: Comparative cross-sectional study. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 11. 257-262.
- Yaribeygi, H., Atkin, S.L., Sahebkar, A. (2020). Molecular mechanisms by which hyperglycemia induces oxidative stress in diabetes. *Journal of Cellular Physiology*; **235(11)**:7594-7607.

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