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Original Article

Association of divalent cations and insulin resistance with thyroid hormones in patients with type 2 diabetes mellitus

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ABSTRACT

Aim: The study was primarily aimed at investigating the association of Magnesium and Zinc levels in the serum of adult Non- obese and Obese type 2 diabetic patients, with particular reference to thyroid comorbidity.

Methods: 108 patients with T2DM of both genders (24 Non obese and 84 Obese) were enrolled from a tertiary health care unit in Puducherry. The cardio-metabolic risk factors were assessed through body mass index, Waist hip ratio, blood pressure, fasting blood glucose, lipid profile and glycated haemoglobin. Zinc and Magnesium were quantitated. Insulin resistance was by Homeostasis model assessment. Serum free T4, T3 and TSH were also measured.

Results: In non-obese type 2 diabetic group, Glycated haemoglobin had a strong positive correlation with free T4($r = 0.784$; $p = 0.003$).TSH also depicted a positive association with HOMA-IR ($r = 0.924$; $p < 0.001$); whereas,T3 and Insulin had negative correlation with Magnesium ($r = -0.599^*$ and $r = -0.620^*$; p 0.04 and 0.031). The levels of Zinc and Magnesium in the serum of obese diabetic patients had a positive correlation among them ($r = 0.565\#$; $p < 0.001$). TAG/HDL ratio a measure of small dense LDL is positively correlated with LDL in both groups ($r = 0.881$ and 0.912) with p value < 0.001 for both.

Conclusion: Correlation among Glycemic control, Insulin resistance, Thyroid hormones, divalent cations and dyslipidemia depict differential characteristics in obese and non–obese type2 diabetes with Thyroid comorbidity.

1. Introduction

Diabetes mellitus, a common endocrine abnormality affects the metabolism of ions including zinc and magnesium [1]. Diabetes affects nearly 170 million people worldwide or 2% of the world's population [2,3]. The proposed mechanism of trace elements enhancing insulin action includes activation of insulin receptor sites, serving as cofactors or components for enzyme systems implicated in glucose homeostasis [4,5]. This increases insulin sensitivity and also act as antioxidants [6]. Lower serum levels of magnesium and zinc are observed in patients suffering from type-2 diabetes [7]. It remains to be seen whether difference in trace element status is a cause or effect. The objective of this study was to assess the levels of Zinc and Magnesium in serum in adult non obese and obese type 2 diabetics, but with reference to thyroid comorbidity, in the light of insulin resistance. This dimension has been envisaged, as thyroid comorbidity is frequently linked to insulin resistance in type2 diabetics and also very few reports from South India are available implicating in obese, overweight and non- obese type 2 diabetes, as the case may be.

2. Methodology

2.1. Inclusion criteria

108 patients with T2DM of both genders (24 Non obese and 84 Obese based on Waist circumference for men 85 cm and for women 80 cm) were enrolled from a tertiary health care unit in Puducherry, during the latter half of 2016, with age in the range 30–75 years. Informed consent was obtained from all the participants. This study was conducted with the approval of the Institutional Human Ethics committee (IHEC).

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2.2. Exclusion criteria

The patients suffering from liver disease, kidney disease, and severe congestive heart failure were excluded from the study. Expecting mothers were also excluded from the study.

3. Biochemical assessment

Fasting blood glucose was estimated by glucose oxidase-peroxidase method (GOD/POD); Fasting insulin was quantitated by automated chemiluminiscence and Glycated hemoglobin by HPLC method. Insulin resistance was measured based on the formula HOMA – IR (Fasting plasma glucose (m mol/l) × plasma fasting insulin (m IU/l)/22.5) [9]. Triacylglycerols in serum was measured by glycerol kinase method; Total cholesterol by enzymatic method; HDL cholesterol was enabled by polyanion precipitation. LDL cholesterol was computed by Friedwald equation, LDL cholesterol = Total cholesterol-(HDL cholesterol + VLDL) where VLDL = TAG/5, Small dense LDL particles were quantitated using the surrogate marker (TAG/HDL); Zinc and Magnesium were estimated using spectrophotometry and T3, T4 & TSH were quantitated based on automated electro chemiluminiscence method. High HOMA-IR was defined as HOMA-IR ≥2.69 [10]. Venous blood was collected from the subjects following an overnight fast. The blood samples (fasting) were analyzed for plasma glucose, insulin resistance by HOMA-IR, lipid profile, glycated haemoglobin, Zinc, Magnesium and T3, T4, TSH. Diabetes mellitus was diagnosed as per American Diabetes Association (ADA) criteria. Glycated haemoglobin less than 7% denoted good Control. For serum lipid reference level, National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guidelines were promulgated [8]. Reference range for Magnesium (serum): 0.7–1 mmol/L i.e. 1.7–2.4 mg/dL; Zinc (serum): 70–100 μmol/L. T4: 0.8–1.8 ng/dL; T3: 2.3–4.2 pg/mL. TSH: 0.4–4.0 mIU/L. All biochemical investigations were performed based on IFCC approved procedures. Internal quality control was enabled. External quality check was facilitated through the External Quality Assessment Scheme (EQAS) scheme promulgated by the Clinical Biochemistry Laboratory, Christian Medical College (CMC), Vellore.

4. Statistical analysis

The statistical tests employed the present study mean ± SD and categorical data enumerated as number (%) percentage. The Pearson correlation coefficient was calculated among the study parameters. The *p*-value <0.05 was considered statistically significant.

5. Results

Table 1 depicts the correlation coefficient of Key parameters as observed in both non obese and obese type 2 diabetics.

The serum Zn and Mg levels were statistically correlated with r value being 0.565, p value <0.001, in obese type 2 diabetic subject as compared to non −obese individuals (Table 1). Fasting glycated haemoglobin level had significant positive correlation with serum level of thyroxine (p 0.003), in non obese type 2 diabetics;while tri iodothyronine had negative correlation (r = −0.599, p 0.04) with Magnesium in the same group; but there was no significant correlation found in obese type 2 diabetics excepting TAG/HDL ratio and Zinc, Magnesium. Insulin was negatively correlated with Magnesium (r = −0.620, p 0.03) in non–obese type 2 diabetics and TSH had strong positive association with HOMA-IR (r = 0.924, p < 0.001) in the same group (non obese). Our study further implies that insulin correlates positively with T3 in non obese. For the sake of clarity, the key parameters are listed on Table 2.

6. Discussion

Type 2 DM is a major global health problem. [11]. It is characterised by insulin resistance in peripheral tissues and an insulin secretory defect of beta cells of the pancreas. The relationship of DM with minerals has been well documented [12–15]. Additionally, zinc may be involved not only in the protection of islet cells, but may also be cardinal to glucose metabolism and insulin signalling. Zinc enables the translocation of insulin into the cells [16]. Additionally, zinc activates the insulin-response amino peptidase (IRAP) molecule, which enables the translocation of GLUT4 to the cell surface for glucose transport into the insulin responsive cells [17]. The clinical significance of trace elements Zinc and Magnesium are of particular interest. Numerous studies have also demonstrated the essential roles of trace elements as chromium, zinc, magnesium, selenium, vanadium, molybdenum and manganese in insulin action and carbohydrate metabolism [18]. In the study undertaken by Almaroof et al., it was observed that mean serum zinc level was significantly low in diabetics as compared to control subjects [19]. A few other studies

Table 2
Key biochemical parameters in the differential manifestation of obese and non obese type 2 diabetes with reference to Thyroid comorbidity.

Parameters	Non obese T2DM	Obese T2DM
T3Vs Mg	r = −0.599*	r = 0.015
Insulin vs Mg	r = -0.620*	r = -0.265
TSH vs HOMA-IR	r = 0.924*	r = 0.019
Zn vs Mg	r = −0.204	r = 0.565*

T3-Triiodothyronine; TSH-Thyroid stimulating hormone; HOMA-IR-Homeostasis model assessment-Insulin resistance; Zn-Zinc; Mg-Magnesium. *pvalue < 0.05.

Table 1
Correlation coefficient between adult non obese and obese type 2 diabetic patients.

	Non obese Type 2 diabetic patients		Obese Type 2 diabetic patients	
Parameters	Correlation coefficient (r)	P value	Correlation coefficient (r)	P value
TAG/HDL vs LDL	0.881#	<0.001	0.912#	<0.001
HbA1c vs T4	0.784*	0.003	−0.283	0.069
T3Vs Mg	−0.599*	0.04	0.015	0.923
T3Vs Insulin	0.620*	0.031	−0.22	0.155
Insulin vs Mg	−0.620*	0.031	−0.265	0.089
TSH vs HOMA-IR	0.924#	<0.001	0.019	0.904
Zn vs Mg	−0.204	0.525	0.565#	<0.001

TAG-Triacylglycerol; HbA1c-Glycated haemoglobin; HDL- High density lipoprotein; LDL-Low density lipoprotein; T3-Triiodothyronine; T4-Thyroxine; TSH-Thyroid stimulating hormone; HOMA-IR-Homeostasis model assessment-Insulin resistance; Zn-Zinc;Mg-Magnesium.
* Indicates statistically significant p value <0.05.
# Indicates statistically significant p value <0.001.