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ESTIMATION OF SERUM CALCIUM AND MAGNESIUM LEVELS IN TYPE-II DIABETES MELLITUS PATIENTS

Biochemistry

Ishtiyak Jafar Post Graduate Student, 3rd year Medical Biochemistry, Department of Biochemistry, Rama Medical College, Hospital & Research centre, Kanpur, U. P.

P. Satyanarayana* Professor, Department Of Biochemistry, Rama Medical College, Hospital & research centre, Kanpur, U. P. *Corresponding Author

ABSTRACT

Type II diabetes mellitus (DM-2) or (Non–insulin-Dependent diabetes) is an endocrinological disease associated with hyperglycemia characterized by both insulin resistance and defective insulin secretion. Macro minerals (calcium, magnesium) play an important role in intermediary metabolism and cellular function, including enzyme activities and electrical gradients. Disturbances in the levels of macro minerals were found to be associated with diabetes mellitus. This study was conducted in 100 subjects, out of which 50 were type II diabetes mellitus patients (case) and 50 were non-diabetic healthy subjects (controls)

- ·Serum was used for the analysis of serum magnesium and calcium.
- · Plasma was used for the estimation of blood glucose.

Out of 50 type II diabetic patients, with 34(68%) male and 16(32%) female, it was found that there is decreases level of serum magnesium and calcium in cases as compared to controls.

The study reveals that there is a significant low level of serum magnesium and calcium in type II diabetic patients which may be an important factor in early onset of the disease in susceptible individuals.

KEYWORDS

calcium, magnesium, type II diabetes mellitus.

INTRODUCTION

Diabetes mellitus ("diabetes") is not one disease, but rather is a heterogeneous group of multifactorial, polygenic syndromes characterized by an elevated fasting blood glucose (FBG) caused by a relative or absolute deficiency in insulin [1].

Diabetes Mellitus is an endocrine disorder which affects over 100 million people worldwide. It is expected that more than one billion people will suffer from diabetes worldwide by the end of the 21st century [2].The disease is characterized by inability of the pancreas to produce sufficient amounts of insulin, or failure of the body's cells to respond appropriately to insulin. In people with diabetes, glucose levels build up in the blood and urine, causing excessive urination, thirst, hunger, and problems with fat and protein metabolism [3].

Non-insulin dependent diabetes mellitus (NIDDM) accounts for approximately 85% all diabetics and can occur at any age. It is most common between 40 to 80 years. In this condition there is resistance of peripheral tissues to the actions of insulin, so that the insulin level may be normal or even high [4]. This type of diabetes is associated with a strong genetic predisposition with patients at an increased risk with an increase in age, obesity, lack of physical exercise, and sustained stress [5].

Macro minerals (calcium, magnesium, chloride, Sulphur and phosphorus) play an important role in intermediary metabolism and cellular function, including enzyme activities and electrical gradients [6]. Serum concentrations of these minerals have been shown to change with plasma glucose levels [7]. Disturbances in the levels of macro minerals were found to be associated with diabetes mellitus [8-10].

Magnesium is an essential element involved in glucose homeostasis. It is a co-factor for various enzymes in carbohydrate metabolism. It is also involved at multiple levels in insulin secretion, binding and activity. Reduced level of magnesium has been documented in type II DM [11-14]. Hypomagnesemia may have negative impact on glucose homeostasis and insulin sensitivity in type II DM patients [15]. Hypomagnesemia may also have some effect in the development of diabetic complications with other risk factors [16].

Intracellular free Mg levels are consistently reduced in subjects with DM- II, when compared with non-diabetic subjects [17-19]. Although the mechanism has not been fully elucidated, an alteration in the mechanism of the Mg uptake in the cells, and/or a deficit of ATP, may help to understand the cellular Mg deficit observed in DM-2 [20]. The relationship between intracellular Mg^{2+} and ATP concentration is rather complex. The decrease in cellular ATP might partially explain the decrease in cellular Mg. Otherwise, a decrease in cellular ATP leads to a decreased binding of Mg^{2+} to ATP in the formation of Mg^{2+}-ATP, which might increase the intracellular Mg^{2+} concentration. DM-2 is frequently accompanied by renal calcium and Mg^{2+} loss [21-22], but the mechanism of this wasting is still not completely elucidated [23].

Serum calcium is a vital mineral for many cellular processes that is tightly regulated by 3 main mechanisms, including renal filtering and reabsorption of calcium, bone turnover, and intestinal absorption of dietary calcium (diet or supplements) [24]. Hyperglycemia causes excess urinary Ca^{2+} excretion in patients with Type- II DM.

Insulin secretion which is a calcium dependent process [25] may alter calcium flux and thus have adverse effects on β-cell secretory function. It may also be speculated that inadequate calcium intake may alter the balance between the extracellular and intra-cellular β-cell calcium pools, which may interfere with normal insulin release, especially in response to a glucose load.

MATERIALS AND METHODS

Upon ethical clearance, this hospital based Case control study was conducted in biochemistry department on **100 subjects, 50** Patients with Type-II Diabetes mellitus **(Cases)** and **50** healthy **controls** in the similar age group, attending OPD of general medicine of Rama Medical College, Hospital & Research Centre, Kanpur, Uttar Pradesh, India. Detailed information of the patients was collected with the help of pre-test proforma that included age, sex and family or personal history of chronic diseases.

INCLUSION CRITERIA

- Subjects between 20–80 years age group were considered.
- Non-Diabetics with normal blood glucose levels were taken as controls.
- Those subjects who have been diagnosed to have diabetes mellitus has been included in study group. i.e., patients with Fasting Plasma Glucose ≥ 126 mg/dl and/or 2 hours Plasma Glucose ≥ 200 mg/dl.

Exclusion criteria

- Age group (<18 years or >80 years)
- Pregnant ladies
- Known cases of Glomerulonephritis, Chronic renal failure, Diuretic therapy, Hyperparathyroidism.
- Smoking and alcoholic individuals
- Patients with history of using drugs that significantly affect glucose metabolism (glucocorticoids, oral contraceptives, high-dose thiazide diuretics)

Method of Analysis:
5ml of fasting blood sample and post-prandial blood sample was collected from antecubital vein into each plain vial and fluoride containing vial from each of the subjects under all aseptic conditions. Serum was used for the analysis of serum calcium and magnesium and plasma was used for the estimation of blood glucose.

Serum Calcium and serum Magnesium were analyzed on Erba Chem 5-*plus* semi-auto analyzer according to the protocol mentioned in the test kits from Erba Mannheim.

- Serum Calcium was estimated by **O-CPC** method.
- Serum Magnesium was estimated by **Xylidyl Blue** method.
- Plasma Glucose was estimated by **GOD-POD** method.

Statistical analysis
All the parameter of case and control were analyzed for mean and standard deviation. The results were expressed as Mean ± standard deviation**.** Data was analyzed using Statistical software i.e. Statistical Package for Social Sciences **(SPSS) version 21.0**.The student t-test was used and the t-value corresponds to a p-value < 0.05 was consider statistically significant. Pearson correlation coefficient was used to find the correlation between the level of Serum Magnesium and Calcium with FBS and PPBS level in Diabetic patients.

RESULTS

1. TABLE 1- Comparison of Diabetic group and Non-Diabetic group based on mean ± std. deviation of age, glucose levels, calcium and magnesium level.

Parameter	Diabetic Group Mean+ Std. Deviation	Non-Diabetic Group Mean+ Std. Deviation	'p' Value
Age	53.35+8.15	45.09+14.07	.001
FBS	199.78+55.02	85.09+8.79	.001
PPBS	284.35+80.12	117.59+8.09	.000
Serum Calcium	7.96+0.31	9.21+0.29	.001
Serum Magnesium	1.11+0.08	2.08+0.07	.000

P value < 0.05, considered as statistical significant.

P value < 0.001, considered as highly significant.

Table-1 shows the Comparison of Diabetic group and Non-Diabetic group based on mean+ std. deviation of age, glucose level, serum calcium and magnesium levels. It was seen that serum calcium and serum magnesium levels significantly decreased in type II Diabetes mellitus when compared to control.

TABLE 2- Pearson Correlation between PPBS level and Serum Calcium level in Type II DM

		N	Pearson Correlation	'p' Value
PPBS	Calcium	51	.055	.699

P value < 0.05, considered as statistical significant.

P value < 0.001, considered as highly significant.

Table-2 shows positive correlation between PPBS level and serum calcium level which is statically not significant.

TABLE 3- Pearson Correlation between PPBS level and serum Magnesium level in Type II DM

		N	Pearson Correlation	'p' Value
PPBS	Magnesium	51	-.035	.806

P value < 0.05, considered as statistical significant.

P value < 0.001, considered as highly significant.

Table-3 shows negative correlation between PPBS level and serum magnesium level which is statically not significant.

DISCUSSION
The aim of this study was comparision between serum calcium and magnesium level among type II diabetic patients. The present study was carried out in 100 subjects, out of which 50 were type II diabetic patients (cases) and 50 were non-diabetic (controls), the levels of serum calcium and magnesium were estimated.

Table-1 indicate the comparison of Diabetic group and non-diabetic group based on mean± std. deviation value of age, glucose levels, calcium and magnesium levels.

Further we observe that the **mean± S. D.** fasting blood sugar (FBS) level in type II diabetic group was **199.78±55.02 mg/dl** and in non-diabetic group was **85.09±8.79 mg/dl.**

Similarly the **mean± S. D.** post-prandial blood sugar (PBS) levels in type II diabetic group was **284.35±80.12 mg/dl** and in non-diabetic group was **117.59±8.09 mg/dl.**

The **mean± S. D.** serum calcium level in type II diabetic group was **7.96±0.31 mg/dl** and in non- diabetic group was **9.21±0.29 mg/dl.** In diabetic patients serum calcium levels were found to be low compared with controls and it is statistically significant (P<0.05). Similarly the **mean±S. D.** serum magnesium level in type II diabetic group was **1.11±0.08 mg/dl** and in non-diabetic group was **2.08±0.07 mg/dl.** It indicate that in diabetic patients levels were found to be low compared with controls and it is statistically significant (P<0.05).

Similar findings were seen in subsequent studies of Vijayalakshmi S et al [25], Marwa AT et al [26], A. Z. Ogunleye etal [27], Kocot et al[28].

Table-2 shows positive correlation between PPBS level and serum calcium level which is statically not significant (P* 0.699 and r * 0.055).

Table-3 shows negative correlation between PPBS level and serum magnesium level which is statically not significant (P* 0.806 and r * -0.035).

In the present study, I obtained a significant decreased in serum calcium and magnesium level in patients having type II diabetes mellitus as compared to control.

Magnesium is a co-factor for various enzymes in carbohydrate metabolism. It is important for the effectiveness of insulin. Magnesium also is deeply involved in the regulation of insulin signaling, in the phosphorylation of insulin receptor kinase, in the post-receptorial action of insulin and in insulin-mediated cellular glucose uptake [16].

Calcium is important for insulin mediated intracellular processes in insulin responsive tissues such as adipose tissue and skeletal muscle with a very narrow range necessary for optimal insulin action. Further calcium is necessary for insulin receptor phosphorylation and proper signal transduction and thus optimal GLUT-4 transporter activity.

Insulin secretion is a calcium dependent process. When blood glucose levels increase the glucose is transported inside with help of GLUT-4 transporters. This glucose is converted to glucose-6-phosphate with aid of glucokinase. This is further oxidized to yield increased ATP which causes closure of potassium channels and hence depolarization of the cell membrane. Depolarization causes increase of calcium flux through calcium channels which causes docking of vesicles containing insulin to fuse with the cell membrane. Insulin is then secreted by exocytosis.

CONCLUSION
From the above studies it was observed that the dysregulation of glucose homeostasis which may alter due to decrease in serum calcium and magnesium levels. It may be concluded that in type II DM, assessment of electrolytes related abnormalities are important to monitor the prognosis of type II DM patients.

This study shows that there is significant decrease in serum magnesium and serum calcium level in type 2 diabetic patients as compared to non-diabetic healthy controls.

The decreased levels of serum Calcium , that were shown in type II DM, may be due to changes in calcium homeostasis, which was represented by Ca^{2+} influx accompanied with this disease. This influx of Ca^{2+} in turn, increases ROS production and oxidative stress.

Thus it can be seen that the role of calcium in the etiopathogenesis of diabetes is multifactorial. If calcium is supplemented along with

vitamin D to diabetic patients it can help in better glycemic control as well as prevent early onset of diabetes if supplemented in non-diabetes subjects.

There are still no consensus regarding of the benefits that Magnesium supplementation can take to the DM patient with and without complication, however the major of clinical studies had demonstrated positive effects on the insulin resistance. In this context it is rational to indicate the supplementation to these patients. It is necessary to accomplish more studies for us to understand better the relation of Magnesium and calcium with the DM II.

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