GLYCEMIC CONTROL AND SERUM MICRONUTRIENTS LEVELS IN TYPE 2 DIABETES MELLITUS- A CASE CONTROL STUDY

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ABSTRACT:

Background: Altered metabolism of some essential micronutrients has been reported in type 2 diabetes mellitus. Hyperglycemia, hyperinsulinemia & increased protein glycosylation observed in diabetics become more pronounced in conditions of poor glycemic states aggravating the serum micronutrients levels. Aims & objectives- To assess the serum levels of calcium, Iron and phosphorus in relation to glycemic control in type 2 diabetes mellitus. **Material & Methods** - This case-control study recruited patients suffering from type 2 diabetes mellitus who came to the department of medicine, of our tertiary care hospital from February 2015 to April 2015.50 patients with type 2 DM, aged 30-65 yrs was recruited as test group. Sociodemographic parameters, age, family history, social history, history of smoking & alcohol, height, weight, BMI, blood pressure were recorded. 5 ml of venous blood was collected by venipuncture and serum levels of calcium, iron and phosphorus were estimated. **Results-** Fasting plasma glucose, HbA1c levels, serum calcium & serum iron levels were statistically significantly higher while serum phosphorus levels were lower in the test group as compared to the control group. Male subjects were observed to have higher phosphorus levels as compared to the female subjects ($p<0.05$). Increased serum Calcium levels and decreased phosphorus levels were observed as age increased in all the study subjects ($p<0.05$). On comparing glycemic control with the various parameters, a statistical difference was observed with higher calcium levels in patients with poor glycemic control ($p<0.05$). **Conclusion-** Diabetes has a significant effect on the metabolism of micronutrients. Serum calcium levels & serum iron levels show an increase while serum phosphate levels decrease. These changes increase with increasing age & variable glycemic control.

Keywords: Hyperglycaemia, Hyperinsulinemia, Protein glycosylation, Micronutrients, Calcium.

INTRODUCTION:

Micronutrients and minerals have an essential role to play in the growth & metabolism of living organisms. Excess or deficiencies of the Micronutrients have been associated as a causative agent in various diseases like diabetes mellitus. Metabolic derangements in diabetic individuals are associated with impaired metabolism & alterations in the serum concentrations of different essential micronutrients. (1) Calcium is required for the secretion of insulin from pancreatic beta cells. Decreased calcium in the body leads to the development of uncontrolled hyperglycemia in type 2 DM. (2) A prospective study reported that the total calcium intake is inversely associated with the incidence of T2DM. Individuals who consumed calcium more than 1,200 mg/day had a 21% decreased risk of developing of T2DM than individuals who consumed less than 600 mg/day. (3)

Previous studies have reported individuals suffering from type 2 DM have lower phosphate levels than healthy individuals. Individuals with poor glycemic control have deranged phosphate levels with increased calcium levels. (4, 5)

Iron plays a significant role in metabolic regulation & pathophysiology of diabetes. Iron overload has been reported in type 2 diabetes.2 Also; the depletion of iron stores has been shown to be associated to a decrease in the risk of developing diabetes. Thus iron levels have an important role in the development of diabetes. Body iron stores have been noted to be positively associated with the development of type 2 DM & gestational diabetes. (6)

Thus, the present prospective study was aimed to assess the serum levels of calcium, Iron and phosphorus in relation to glycemic control in type 2 DM.

MATERIAL & METHODS

This case-control study recruited patients suffering from type 2 DM who came to the department of medicine, of our tertiary care hospital from February 2015 to April 2015.50 patients with type 2 DM, aged 30-65 yrs was recruited as test group. 50 apparently healthy individuals were taken as the controls. Written informed consent was sought from all the subjects & institutional ethical approval taken.

Patients suffering from hypertension & pregnant females were excluded.

On the day of sample collection, sociodemographic parameters, age, family history, social history, history of smoking & alcohol, height, weight, BMI, blood pressure were recorded.

Subjects were instructed to report in the fasting state in the morning of the day for sample collection. 5 ml of venous blood was collected by venipuncture and serum levels of calcium, Iron and phosphorus were estimated.

BMI between 18-25 kg/m2 was considered normal, while obesity was considered when BMI >30 kg/m2. HbAlc levels <7.0% was considered as good glycemic control while HbAlc >8.0% were considered as poor glycemic control.

Statistical analysis

The tabulated data was statistically analyzed using SPSS version 22.0 for Windows (IBM Corp, India). Quantitative data are presented as mean ± SD or proportions. Intergroup comparisons were made using Student's paired *t*-test. Pearson correlation coefficient was used to analyse the relation between the variables. A P-value of 0.05 at a 90% confidence interval was considered to be statistically significant. Values were expressed as number (n) and percentage (%).

RESULTS

The mean age, BMI, Systolic blood pressure and diastolic blood pressure were comparable in both the test group & control group. Fasting plasma glucose, HbA1c levels, serum calcium & serum iron levels were statistically significantly higher while serum phosphorus levels were lower in the test group as compared to the control group. Male subjects were observed to have higher phosphorus levels as compared to the female subjects ($p<0.05$). Increased serum Calcium levels and decreased phosphorus levels were observed as age increased in all the study subjects ($p<0.05$). No significant differences in levels of other parameters were observed with respect to age or gender ($p>0.05$). On comparing glycemic control with the various parameters, a statistical difference was observed with higher calcium levels in patients with poor glycemic control ($p<0.05$).

Table 1 Comparison of Parameters between Test Group and Control Group

Parameters	Test Group	Control Group	p value
Age	55.62 ± 09.22	56.71 ± 10.27	>0.05
BMI	24.68 ± 5.52	25.77±6.29	>0.05
Systolic blood pressure	127.70 ± 6.42	128.63± 7.81	>0.05
Diastolic blood pressure	81.60 ± 9.60	80.20±10.70	>0.05
Fasting plasma glucose	8.73 ± 4.27	4.47 ± 0.23	<0.05
HbA1C	9.87 ± 3.46	4.97 ± 1.03	<0.05
Ca	2.52 ± 0.03	2.31 ±0.02	<0.05
Phosphorous	1.34 ± 0.04	1.79 ± 0.05	<0.05
Iron	25.44 ± 1.59	17.54 ± 0.78	<0.05

DISCUSSION

Calcium plays a vital role in many biological processes; it is available in free ion form or bound complex form. It provides skeleton strength & maintains intra- and extracellular calcium pools for extra- and intracellular signaling, nerve impulse transmission & muscle contraction. Calcium homeostasis is largely maintained by parathormone & Vitamin D.**(7)** In the present study ,increased calcium levels were observed in the test group with type 2 DM, with increasing levels in patients with poor glycemic control as compared to the control group which was statistically significant ($p<0.05$). This is in accordance with studies conducted by Yamaguchi T 2011, which observed that the serum Ca levels were significantly and positively correlated with fasting plasma glucose after adjustment for serum parathormone & other variables in T2DM men. Serum PTH levels were not found to be correlated to any diabetic related parameters after adjustment for serum Ca in either sex. Thus the findings suggest that serum Ca was involved in the aggravation of hyperglycemia and insulin resistance in T2DM men & was linked to impaired glucose metabolism in T2DM men.**(8)** Also , Sun et al observed that serum Ca was statistically significantly correlated with glucose and insulin resistance in non-diabetics after adjustment for vitamin D and parathormone.**(9)** Tomas NB et al 2014, noted increased serum calcium levels to be associated with an increased risk of type 2 DM in individuals at high cardiovascular risk. **(7)**

In the present study, serum iron levels were statistically significantly higher in the test group as compared to the control group. Insulin results in significant stimulation of iron uptake by the adipose tissues through redistribution of transferrin receptors to the cell surface. Transferrin receptors have been shown to coexist with glucose transporters in the microsomal membranes of cultured adipocytes. This shows that regulation of glucose metabolism & iron uptake occurs simultaneously. Cultured rat glioma cells demonstrated increased ferritin synthesis due to the effect of insulin. Thus increase in insulin secretion in type 2 DM will

lead to a corresponding increase in iron uptake & rise in ferritin levels. **(6)**

According to a study by Jiang R 2004, a strong relationship was found between ferritin and diabetes risk, when factors like age, race, alcohol, smoking, and inflammatory state were controlled. **(10)** High ferritin was also positively correlated with central adiposity **(11)**, hepatic steatohepatitis **(12)**, and cardiovascular disease **(11)**.Type 2 diabetes is a disease with marked chronic inflammation **(13)**, and ferritin increases with inflammation. Cooksey et al 2010 observed low iron diets or iron chelators resulting in decreased risk of diabetes owing to an increased insulin secretion and sensitivity.

In the present study, low serum phosphorus levels were observed in the test group as compared to the control group. Study by Nsonwu-Anyanwu AC et al. 2015 observed low phosphorus levels in diabetics when compared to the control group.(15) Also changes in serum phosphate levels have been shown to relate to the severity of DM.**(16)** In type 2 DM metabolic disturbances cause an imbalance in inorganic phosphate which causes decreased high energy phosphate and tissue hypoxia.**(17)** Due to hyperglycemia, there is altered homeostasis in the kidney , resulting in glycosuria inducing depolarization of the brush border membrane, facilitating reabsorption of inorganic phosphate & lack of intracellular phosphate and hyperphosphaturia.**(17)**

Secondly, during hyperglycemic states, high amounts of glucose enter muscle and fat tissues. This intracellular glucose undergoes phosphorylation, leading to a reduction in plasma phosphate levels.16Males have higher inorganic phosphate levels compared to the females while phosphate levels decreased with increasing age. **(18)**

CONCLUSION

Thus the findings of the present study conclude that diabetic metabolic syndrome has a significant effect on the metabolism of micronutrients. There is an increase in serum calcium & serum iron levels whereas the serum phosphate levels are lowered. Such changes are aggravated with increasing age & variable glycemic control. Measures should be taken further to prevent the risk of atherosclerotic stroke, kidney failure & other debilitating diseases.

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