A STUDY OF MUTUAL INTERPLAY OF MICRONUTRIENTS AND SPECTRUM OF DIABETIC PATIENTS

Diabetology

Dr. Roopal Verma	MBBS, DNB. Senior Resident, Department of internal medicine, Sir Ganga Ram Hospital, New Delhi.
Dr. Aanchal Sawhney*	MBBS, Junior Resident, Rajiv Gandhi Cancer Institute, New Delhi.*Corresponding Author
Dr. Mridusmita Khataniar	MBBS, DNB, Senior Resident, Department of internal medicine, Sir Ganga Ram Hospital, New Delhi.

ABSTRACT

Persistent uncontrolled hyperglycaemia in Diabetes Mellitus causes permanent structural and functional damage to tissues, which leads to micro and macro vascular complications causing increased mortality and morbidity. Magnesium and Calcium are required for Insulin secretion, Iron is essential for cell functioning and zinc forms the structure of insulin. 90 subjects were enlisted in the study after obtaining written informed consent and divided into 3 groups of pre-diabetic, diabetic and diabetic with micro and macro vascular complication. A brief history with relevant clinical examinations using monofilament test and ophthalmoscopic examination were done to evaluate for diabetic neuropathy and retinopathy respectively. Blood samples for serum zinc, calcium, magnesium and iron were collected and analysed with respect to age, gender and duration since diabetes was diagnosed. With increase in duration of diabetes and HbA1c, serum zinc, iron, and magnesium levels decreased, while calcium levels increased. Till date very few studies have been conducted to study micronutrients deficiency in pre-diabetics. Detection of micronutrients deficiency early in the course of diabetes, may delay the development of complications with their supplementation. Hence, this study is being done to study micronutrients in diabetics and pre-diabetic patients.

KEYWORDS

Micronutrients, Pre-diabetes, Diabetes, Zinc

INTRODUCTION

Persistent hyperglycaemia of uncontrolled diabetes is known to cause an alteration in the metabolism of some micronutrients which leads to a vicious cycle of disturbed micronutrients and glucose homeostasis. Some trace elements such as zinc, magnesium, manganese, and selenium potentiate the blood glucose lowering effect of insulin through insulin receptors activation, cofactors, or through antioxidant properties. (1). Many studies have suggested that alteration in the metabolism of these macro and trace elements may be a causative factor for development and progression of diabetes mellitus (2). 90 patients in our study were divided into 3 groups according to ADA guidelines (3).

DiSilvestro in his article on zinc explained that deficiency of zinc might lead to decreased synthesis and secretion of insulin from pancreatic beta cells in diabetes mellitus. (4) A study conducted in Japan showed that autoantibodies against zinc transporter were present in 50 – 60% population who had recent onset diabetes mellitus. (5) Iron is a component of antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. Oxidative stress is found in diabetes and its complications. (6) Abnormally high blood glucose can cause non-enzymatic glycation of the amino acids found in a protein which produces advanced glycation end products which play an important part in development and progression of diabetes and its complications. (7) Higher levels of serum iron found to be associated with insulin resistance, diabetes mellitus, and its vascular complications.

Magnesium is a micronutrient that is necessary for formation, secretion of insulin and acts as a cofactor for several enzymes involved in normal glucose metabolism. (8) Hypomagnesaemia has been linked to poor glycaemic control, diabetic nephropathy, neuropathy and diabetic retinopathy. (9) Uncontrolled hyperglycaemia also causes reduced efflux of calcium from cells. This increase in calcium entry and decreased exit from the cells results in high concentration of calcium in the cells. (10)

Whether these micronutrients are affected in people with impaired fasting glucose or impaired glucose tolerance is not very evident, as not many studies have been done in these subsets of patients. Hence, this work was undertaken to evaluate levels of serum zinc, iron, magnesium and calcium in prediabetic and in diabetic patients with and without micro vascular complications.

AIMS AND OBJECTIVES

1. To estimate and compare serum zinc, iron, magnesium, and

calcium level in prediabetes and diabetes mellitus patients with and without micro vascular complications.

2. To study association of age, glycaemic status, and duration of disease with the serum concentration of these micronutrients in these subjects.

MATERIAL AND METHODS

In an observational comparison conducted in a tertiary care hospital in North India over 17 months, 90 subjects were enlisted in the study after obtaining written informed consent. These subjects were divided into 3 groups each consisting of 30 people namely, group 1 prediabetic patients, group 2 diabetic patients without complications while group 3 had a population of diabetic patients with micro vascular complications.

Inclusion criteria:

1. Diagnosed cases of prediabetes on the basis of ADA criteria for prediabetes for group 1.
2. Diagnosed cases of type 2 diabetes mellitus on basis of ADA diagnostic criteria for diabetes for groups 2 and 3.
3. Patients of age group (18-60 years) for all the three groups.
4. Subjects consenting to be a part of the study.

Exclusion criteria:

1. Subjects with malabsorption syndrome, diarrhoea, pancreatitis, alcoholism, liver disease, chronic renal failure due to factors other than diabetes.
2. Patients with retinopathy or neuropathy due to factors other than diabetes.
3. Patients who were pregnant.
4. Subjects taking micronutrients supplementations.

A brief history with relevant clinical examinations using Monofilament test and ophthalmoscopic examination were done to evaluate for diabetic neuropathy and retinopathy respectively. Blood and urine samples were collected for HbA1c, serum zinc, iron, magnesium, and calcium and detection of micro albumin respectively. Data collection and analysis was done hereafter.

The reference range for iron was 50-160 µg/dl in male and 40-150 µg/dl in the female, for calcium was 8.2-10.4 mg/dl, for Zinc was 80-120 µg/dl and for Magnesium was 1.7-2.7 mg/dl. (11)

RESULTS

115 patients were enrolled and finally 90 patients were recruited due to

refusal and exclusion criteria out of which 30 patients were divided equally into prediabetic, diabetic and diabetics with complications. Of the 90 subjects, 48 were females (53.33%) and 42 were males (46.67%). In our study, with increasing age, the levels of serum magnesium showed a decreasing trend however, age had no effect on serum levels of zinc, iron and calcium levels.

In this study, the serum zinc, magnesium and iron were normal in pre-diabetic population and showed a decreasing trend in diabetics with and without complications. On the contrary, serum calcium was normal in pre-diabetics and showed increasing trends in diabetics with and without complications. Similar decreasing trends in serum zinc, magnesium and iron levels were observed in patients with increase in duration of diabetes and HbA1c levels, however serum calcium followed a decreasing trend with increasing duration of diabetes and HbA1c levels in the above mentioned groups.

DISCUSSION

Micronutrients play a vital part in the pathogenesis of Diabetes. The serum zinc values showed a decreasing trend across the groups, which may be due to increased loss in urine. Contrary to our study, a previous study done by Rafiqul et al showed a lower level of serum zinc in prediabetics compared to normal and diabetic subjects. (12) Results similar to our study were found in a study done in Punjab, in which low zinc levels were seen in all diabetic patients but the decrease in levels was more in the group with microangiopathic complications. (13)

The mean serum iron values showed decreasing trends of serum iron across the groups. Similar results were found in a study done in Iranian elderly population with significantly low levels of serum iron in diabetic group in comparison to the normal population (14) Mean serum magnesium in group 1 was normal and a decreasing trend was seen in groups 2 and 3. The previous study done by Stricker et al showed low magnesium levels in prediabetics. (15) Mean serum calcium was above the reference range in all groups and a significant difference was found in between the groups. Shimodaira et al also concluded in their study that the albumin-adjusted calcium levels were high in prediabetics. (16) They also observed that higher levels of serum calcium were associated with complications of diabetes.

With respect to age, levels of serum magnesium showed a falling trend with increasing age whereas age had no effect on serum levels of zinc, iron, and calcium. Similar results were explained by Masood et al in their study. (17) In our study, duration of diabetes and HbA1C also had a significant effect on micronutrients levels. With an increase in duration of diabetes and HbA1c levels, serum zinc, iron, and magnesium levels decreased, while calcium levels increased.

Correlation study showed a statistically significant negative correlation in between age and serum magnesium among prediabetics (group 1). Among group 2 statistically significant positive correlation found in between HbA1c and serum calcium. A study conducted by Kanchana et.al. in Chennai showed a negative correlation between serum calcium levels and blood glucose levels. (18) Among group 3, a statistically significant positive correlation was seen in between age and serum magnesium and in between HbA1c and serum calcium.

CONCLUSION

Our study suggests that Zinc, iron and magnesium deficiencies are significantly more commonly seen in diabetics with or without complications. Calcium levels, on the other hand, are seen to significantly increase with the disease and its complications. Micronutrients are not a part of mainstream management of diabetes as of 2018. However, as diabetic care advances, in the near future these may become a part of holistic management of the disease and its complications. These alterations in micronutrient levels suggest an intricate relationship of these with diabetes, its duration and its complications and hold promise as a potential avenue of therapeutics in managing this burgeoning disease more effectively.

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