Evaluation of serum magnesium and zinc levels in patients with Type 2 diabetes mellitus

Dhananjay Tiwari[1,*], Narendra Kumar[2], Roshan Alam[3], Mohammad Mustufa Khan[4]

[1]Assistant Professor, [3]Professor, [4]Research Scholar, Integral Institute of Medical Sciences & Research, Integral University, Lucknow, Uttar Pradesh, [2]Tutor, Dept. of Biochemistry, Prasad Institute of Medical Sciences, Lucknow, Uttar Pradesh

***Corresponding Author:**
Email: tiwarivaranasi@gmail.com

Abstract

Introduction: The complications of Type 2Diabetes, both microvascular and macrovascular develop at an early stage of life in Indian population. The reasons may be poor glycemic control and excessive loss of serum Mg and serum Zn.

Aim: To estimate the serum magnesium and serum zinc levels in type 2 diabetes mellitus (T2DM) patients.

Materials and Method: In the present case-control study, we inducted 94 subjects (47 T2DM and 47 age and sex matched healthy controls), aged between 25-70 years. Fasting blood sugar (FBS), post prandial blood sugar (PPBS), glycated haemoglobin (HbA1c), serum Mg and serum Zn were estimated in each of them. Statistical analysis was conducted by using SPSS version 20. Results were tested at 5% level of significance.

Result: Level of serum Zn was found low in T2DM patients compared to healthy controls and the difference was statistically significant ($p=0.03$), whereas, there was no significant difference in serum Mg levels ($p=0.14$). FBS, PPBS and HbA1c have significant positive correlation in T2DM patients ($p<0.01$). Mg has shown negative correlation with FBS, PPBS and HbA1c. While, it showed positive correlation with Zn. However, Zn has shown positive correlation with FBS and PPBS, while negative correlation with HbA1c. All the correlations were found to be not significant.

Conclusion: In the present study, the serum zinc level was low in Type 2 DM patients in comparison to healthy controls. The difference was statistically significant. However serum magnesium levels were not significantly different in T2DM in comparison to healthy controls. The reduced serum zinc levels in T2DM patients may be due to gastrointestinal malabsorption and excessive urinary loss of zinc.

Keywords: Magnesium, Zinc, HbA1c, Type 2 Diabetes Mellitus

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Introduction

Diabetes mellitus is a group of common metabolic diseases that display the phenotype of hyperglycemia.[1] The chronic hyperglycemia associated with diabetes leads to long-term damage and ultimately failure of various organs e.g. kidneys, nerves, heart.

According to the International diabetes federation by 2015, Some 415 million people worldwide, or 8.8% of adults aged 20-79, are estimated to have diabetes. By 2040, around 642 million people, or one adult in ten, will have diabetes. According to IDF 2015, in India there are 69.2 million people suffering from T2DM.[2]

Some trace elements like zinc and magnesium are important for human growth and body's biological functions. They commonly function as cofactors for metabolic reactions and thus support basic cellular reactions required to maintain energy production.[3] Magnesium is the second most prevalent intracellular cation. The total body magnesium is approximately 25g, of which around 55% resides in the bones and 45% in soft tissues. It also serves as cofactor for more than 300 enzymes.[4,5] In particular, magnesium plays salient roles in such biologic processes as: energy metabolism and production, synthesis of nucleic acids and proteins, cytoskeletal function, cell cycle progression, maintenance of membrane integrity and stability, and ion homeostasis.[6] Magnesium may contribute to the pathogenesis of diabetic complications and increased risk of sudden death in diabetic patients.[7] Hypomagnesemia is common in patients hospitalized with hyperglycemia. Ten percent of the patients admitted to city hospitals and as many as 65% of patients in intensive care units may be hypomagnesemic. Moderate or severe magnesium deficiency is usually due to losses of magnesium from gastrointestinal (GI) tract or kidneys. More commonly, magnesium deficiency is associated with losses from the lower intestine.[8]

Zn occurs in more than 300 metallo-enzymes in all six categories of enzyme systems. It plays an important role in the maintenance of several tissue functions, including the synthesis, storage and release of insulin. Zinc enhances the effectiveness of insulin in vitro, and it has been postulated that zinc deficiency may aggravate the insulin resistance in non-insulin dependent diabetes mellitus.[9] In most mammals, insulin is stored in association with zinc crystals.[10] Zinc is also required for normal immune function, taste acuity and enhances the in vitro effectiveness of insulin. Impaired immune function is well documented in diabetic subjects, and decreased serum zinc levels and hyperzincuria occur in some diabetic subjects.[11] Hypozincaemia and

hyperzincuria is known to be present in patients of both T1DM and T2DM.

Measurement of zinc and magnesium status is not frequently suggested to diabetic patients and clinical trials with zinc and magnesium supplementation in diabetic subjects are very small and have yielded inconsistent results. Hyperglycemia from either type of diabetes mellitus causes physiologically significant losses of zinc from the body. These losses may be due to the underlying diabetes but are probably not responsible as the causal agents. However, studies on zinc and magnesium level with regard to diabetes mellitus have given conflicting results.

Materials and Method

Subject Selection: This is a case-control study and all subjects (T2DM and healthy controls) were enrolled from outpatient Diabetes Clinic of IIMS & R, Integral University, Lucknow (India). Study was approved by ethical committee of the institution. Written informed consent was taken from each subject and all procedures performed in this study were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.[12]

This study was conducted on 94 subjects (47 T2DM and 47 healthy controls), aged between 25-70 years. T2DM was defined according to the criteria provided by World Health Organisation [13]

Subjects with ischemic heart disease, abnormalities on electrocardiogram, those with other concurrent illness or those on drugs like diuretics and women using oral contraceptives were excluded.

Anthropometric parameters

BMI Estimation: Weight was recorded to the nearest kilogram (kg) with the subject standing on the weighing machine with minimum of clothing.[14]

Height was recorded, with a height measuring instrument, with the subject erect; bare footed; feet together; back and heels against the upright bar of height scale; head upright in Frankfort horizontal plane, looking straight ahead.[15]

Body Mass index was calculated from the formula; [BMI= Weight in Kilogram/ (Height in meters)^2]

Asian Indians tend to develop diabetes at a significantly lower BMI and WC than white Europeans, lower thresholds of BMI to define overweight (BMI: 23-24.9 kg/m^2) and obesity (BMI $\geq$ 25 kg/m^2) were proposed by NICE guidelines for Asian Indians.[16]

Laboratory investigations: 5 ml venous blood was collected after overnight fast. Fasting and post prandial blood sugar were estimated in Siemen's Dimension RXL max fully automated analyser. Serum Mg and Zn were estimated in semi auto analyser (meridian). HbA1c was estimated by Nephelometry based method using Mispa-*i*.

Statistical Analysis: Statistical analysis was done using SPSS software version 20.0 (Armonk, NY, USA). Unpaired t-test were used for comparison of phenotypic data. Values were expressed in mean ± SD (Standard Deviation). Pearson correlation coefficient was calculated in T2DM patients. All the data were tested at 5% level of significance.

Results

In this study, 47 Type 2 DM patients aged between 25-70 years and 47 controls of same age group and sex were included. The mean age of T2DM patients and controls were (48.31±10.88 years) and (48.03±11.83 years) respectively. Sex wise distribution showed 27 male and 20 female in T2DM and 25 males and 22 females in controls. The serum levels of FBS, PPBS and HbA1c were estimated in both groups. Serum magnesium and zinc levels were also measured in both groups along with BMI.

Table 1 shows that FBS, PPBS and HbA1c are significantly increased in patients with T2DM in comparison to healthy controls ($p<0.001$, $p<0.001$, $p<0.001$, respectively). Serum level of Zn was low in T2DM patients compared to healthy controls and the difference was significant ($p=0.03$). However, there was no significant difference in BMI and serum Mg levels ($p=0.14$, $p=0.14$, respectively). Table 2 shows FBS, PPBS and HbA1c have significant positive correlation in T2DM patients ($p<0.01$). Serum Mg has shown negative correlation with FBS, PPBS and HbA1c. However, it showed positive correlation with Zn, but none of them were significant. Zn has shown positive correlation with FBS and PPBS, while negative correlation with HbA1c, but the correlations were not significant.

Table 1: Clinical and anthropometric parameters of T2DM cases and control groups

Parameters	T2DM (n=47)	Control (n=47)	P-value
AGE (years)	48.31±10.88	48.03±11.83	0.83
Gender (M/F)	27/20	25/22	0.84
BMI (Kg/m^2)	22.76 ±3.91	21.37± 1.64	0.14
FBS (mg/dl)	250 ±120	80 ± 10.47	<0.001*
PPBS (mg/dl)	322 ±124	127± 9.99	<0.001*
HbA1c %	8.44 ±2.10	4.99± 0.5	<0.001*
Mg (mEq/L)	1.69 ±0.42	1.88± 0.54	0.14
Zn (µg/dl)	67.88 ±28.02	83.23± 14.52	0.03*

Values are expressed as Mean ± Standard Deviation
**Significant considered as P<0.05.*
M: Male, F: Female, FBS: Fasting Blood Sugar, PPBS: Post-Prandial Blood Sugar, HbA1c: Glycated Haemoglobin, BMI: Body Mass Index

Table 2: Pearson correlation coefficient among the study parameters in T2DM cases

Parameters→↓	FBS	PPBS	HbA1c	Mg	Zn
FBS	1	0.925**	0.574**	-0.320	0.000
PPBS	-	1	0.538**	-0.287	0.031
HbA1c	-	-	1	-0.169	-0.206
Mg	-	-	-	1	0.231
Zn	-	-	-	-	1

**Correlation is significant at the 0.05 level (2-tailed)*
***Correlation is significant at the 0.01 level (2-tailed)*

Discussion

In the present case-control study, we inducted T2DM patients along with age and sex matched healthy controls. In T2DM, male-female ratio was 1.35 and in healthy controls it was found to be 1.14. The mean BMI of T2DM patients (22.76 ±3.91) was found slightly higher than healthy controls (21.37± 1.64), however the difference was not significant. This indicates that T2DM patients have low BMI although mostly they are middle aged patients. Various studies were reported that Asian Indians have constantly low BMI in diabetic patients and they are more prone for the risk of cardiovascular disease at lower BMI.[17,18]

The clinical parameters of T2DM patients like FBS, PPBS and HbA1c were found significantly raised as compared to healthy controls. Previous studies have shown that blood sugar levels were significantly raised in T2DM patients as compared to healthy controls.[19] Chronic hyperglycemia in patients with diabetes predisposes them to early development of microvascular and macrovascular complications.[17,19]

In this study, serum magnesium level was not significantly different (p=0.14) between control subjects and diabetic patients. The findings are similar with those of Masood et al. which has shown no difference in plasma magnesium level between control subjects and diabetic patients.[20] However, several studies have reported that serum magnesium was significantly low compared to the controls.[10,11,21] The reason may be, polyuria, as seen in diabetes mellitus, can affect corporal concentration of magnesium, developing hypomagnesaemia which may still be related directly with some micro vascular and macro vascular complications observed in diabetes mellitus.[22] Jaswant et al. stated whether magnesium depletion is a cause or consequence of T2DM remains debatable, but magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with T2DM.[21] According to Ferdousi et al. the reasons of decreased magnesium in T2DM are not clear, but may be due to raised urinary losses or malabsorption of magnesium as compared to healthy controls. The fall in serum magnesium may also be due to diuresis (osmotic), and circumlocutory hormonal effects.[10]

Also, level of Zn was found significantly low in T2DM patients in comparison to controls (p=0.03). There was no significant difference in Mg and BMI levels (p=0.14, p=0.14, respectively). Many previous studies reported similar results.[21,23,24] One explanation for reduced serum zinc levels in diabetic patients is excessive urinary loss of zinc especially in patients with diabetic nephropathy, gastrointestinal malabsorption or genetic factors.[23] According to Jaswant et al. the possible explanation for decreased level of zinc observed in diabetics can be due to increased urinary loss and/or decreased gastrointestinal absorption of zinc. In contrast, Rusu et al. showed that the levels of zinc in diabetic patients were equal to or higher than that of control groups. Rusu et al. attributed the presence of vascular complications as a cause of higher level of serum zinc concentration in diabetic persons.[25]

FBS, PPBS and HbA1c have significant positive correlation in T2DM patients (p<0.01). Mg has shown negative correlation with FBS, PPBS and HbA1c. However, it showed positive correlation with Zn, but the correlations were not significant. Zn has shown positive correlation with FBS and PPBS, while negative correlation with HbA1c, but not significant. Anetor et al. have reported that the concentrations of both Mg and Zn were significantly low, however Mg and Zn were not significantly correlated with blood glucose.[26] Badran et al. also confirmed by multivariate statistical analysis that the altered levels of some essential trace metals may play a role in the pathogenesis of diabetes mellitus.[27]

On the basis of present findings, Zinc supplementation is known to be helpful in restoring plasma Zinc levels to normal.[28,29,30,31] Zinc supplementation enhances the activity and levels of key anti-oxidant enzymes and proteins, while significantly reducing lipid peroxidation.[32]People with uncontrolled diabetes have increased zinc losses in the urine. Ordinarily, these losses are counterbalanced by enhanced zinc absorption in the gut.[33, 34]

Abnormal zinc and lipid levels occur more frequently in metabolically uncontrolled diabetic subjects. These lipid abnormalities are key factors in the emergence of cardiovascular complications. Significantly reduced total cholesterol and triglycerides concentrations and elevated HDL correlate to zinc levels.[35] Small studies in older subjects with diabetes have suggested some benefit in healing skin ulcerations with zinc supplementation.[33, 34, 36]

Conclusion

In this study, the serum zinc level was significantly low in Type 2DM patients in comparison to healthy controls, whereas serum magnesium levels were not significantly different between Type 2DM and healthy controls. The decreased serum zinc level in T2DM patients may be due to decreased gastrointestinal absorption and excessive urinary excretion of zinc.

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