To study the effect of age and blood sugar on the levels of magnesium and glycated hemoglobin in Bundelkhand region: A case control analysis

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Abstract

In Type 2 Diabetes Mellitus (T2DM) loss of minerals may lead to decrease in its bodily content and might affect the concentrations of minerals. The aims of this study were to compare the plasma glucose, glycated hemoglobin (HbA1c), and Magnesium (Mg) concentrations of patients with T2DM and healthy controls (Non-diabetic) in Bundelkhand region and also to know the association of blood glucose and HbA1c with Mg in respective groups. This study has shown altered Fasting Blood Sugar (FBS), HbA1c, and Mg in T2DM group subjects when compared with healthy control group subjects. The statistical significance was observed to be at p<0.05. Insignificant difference was observed in the age parameter when compared between the two groups. In the present study pertaining to T2DM group subjects, an inverse correlation between Age and FBS; Age and HbA1c were established. In conclusion, we observed lower Mg levels in T2DM individuals in the Bundelkhand region. As Mg depletion aggravates insulin resistance and may result in increased loss through urine, therefore, it may be advisable to periodically monitor Mg concentrations in T2DM subjects. Moreover, further research is imminent to understand the deeper insights into the association of Mg with T2DM which is, prior to the initiation or after initiation of T2DM.

Introduction

Type 2 Diabetes Mellitus (T2DM) is a metabolic disorder in which there is insulin resistance, and it is experienced by insulin dependent tissues and for the same insulin is needed for the uptake of glucose[1]. The classical symptoms of T2DM include increased thirst, frequent urination, and unexplained weight loss[2]. Long-term persistent hyperglycemia leads to a number of secondary complications due to glucose toxicity namely cardio-vascular diseases, cerebral strokes, diabetic nephropathy, peripheral neuropathy and diabetic retinopathy which can result in loss of vision[3,4]. There are many etiologic hypotheses for hyperglycemia in T2DM, such as genetic defect[5], loss of insulin sensitivity[3], High Density Lipoprotein (HDL) defect[6], oxidative stress[4], glucose toxicity[3,4], low concentrations of chromium[7,8], zinc[9], and melatonin[10,11]. It is possible that several of these hypotheses, e.g., trace element deficiencies[7-9], mitochondrial defect[12], and oxidative stress[3] may interact as pathogenetic mechanisms for insulin resistance in T2DM. Bioavailability of minerals is hampered in hyperglycemia due to change of oxidation state of minerals for their vulnerability towards free
radicals\textsuperscript{[13]}. Loss of minerals may lead to decrease in its bodily content and might affect the concentrations of minerals like Magnesium (Mg). Mg is a necessary co-factor for several enzymes that play a vital role in glucose metabolism\textsuperscript{[14]}. Studies have demonstrated hypomagnesemia as a common feature in patients with T2DM\textsuperscript{[15]}, though diabetes can induce lower Mg levels, in addition, Mg deficiency has been proposed as a risk factor for T2DM\textsuperscript{[16]}. Studies on models demonstrated that Mg has a negative effect on the signaling process of insulin\textsuperscript{[17,18]}. However, some studies\textsuperscript{[19,20]} revealed that Mg administration has a beneficial effect on insulin action and glucose metabolism. In a study\textsuperscript{[21-23]}, found an inverse correlation between Mg intake and risk of T2DM. Moreover, Mg depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with T2DM\textsuperscript{[24,25]}, as well as on the evolution of complications such as retinopathy, thrombosis and hypertension\textsuperscript{[26,27]}. Interestingly, a study showed lower serum Mg is a strong independent predictor of the development of T2DM\textsuperscript{[28]}. In a country it has been shown that nearly 40% outpatient diabetics have low concentrations of serum Mg\textsuperscript{[29]}, and several studies have shown lower serum Mg concentrations in T2DM compared to healthy controls\textsuperscript{[30,32]}. However, there is no clear indication or hypothesis to trace whether Mg deficiency occurs first or after development of T2DM. Although low serum Mg concentrations in diabetics have also been found in several studies\textsuperscript{[14-32]}, there are no reported data for diabetics living in Bundelkhand region. Therefore, the aims of this study were to compare the plasma glucose, glycated hemoglobin, and Mg concentrations of patients with T2DM and healthy controls in Bundelkhand region and also to know the association of blood glucose and HbA1c with Mg in respective groups.

### Materials & Methods

The study was conducted in the Department of Biochemistry, Maharani Laxmi Bai Medical college (MLBMC), Jhansi. Age & sex matched fifty human individuals having a normal glycaemic status were taken into healthy control group. Fifty T2DM subject, on treatment were included in T2DM group. The diagnosis of T2DM was made according to the norms laid by American Diabetes Association 2018. The diagnosis of T2DM group subjects was done by the consultants of General Medicine department of MLBMC. Exclusion criteria were type 1 diabetes individuals, less than five years of known duration of T2DM, and with complications. Inclusion criteria for healthy controls were non-diabetic, not taking supplementations, and having no other complications. Fasting venous blood (5ml) were drawn into EDTA and plane vials, after informed written consent from all the study group subjects with a disposable syringe & needle, under all aseptic conditions. Serum was separated by centrifuging the blood at 3000 rpm for 20 minutes. Samples were stored in aliquots at -20° C until assayed. Plasma glucose was estimated by using the method Glucose Oxidase and Peroxidase (DPEC – GOD/POD) purchased from Transasia Biomedicals. HbA1C was estimated by using the ClinRep complete kit on the BioRad HbA1c analyzers Diamat and Variant. Serum Mg was estimated by using the method of Calmagite purchased from Beacon Coral Clinical Systems.

### Statistical Analysis

Unpaired ‘t’ test was performed to compare the means of variables between T2DM group and healthy control group subjects. Scattered plots were used to know the regression equation of variables taken in the present study and were considered to understand the association between two variables. P <0.05 was considered significant.

### Results

The figures 1 and 2 show altered FBS and HbA1c, and Mg in T2DM group subjects when compared...
with healthy control group subjects. The statistical significance was observed to be at p<0.05. Insignificant significant was observed in the age parameter when compared between the two groups.

Insignificant differences were reported in the age (53.9±7.2) and (53.06±4.7) and in the distribution of subjects in the age groups of 41-50, 51-60, 61-70, and above 70 years when compared between the Type 2 Diabetes Mellitus (T2DM) subjects and healthy controls of the present study (Figs. 3 & 4). Only one subject was included above 70 years of age as per our criteria.

In the present study pertaining to T2DM group subjects, an inverse correlation between Age (x axis) with FBS; Age and HbA1c were established as evident from the graph shown in the figure 3. In addition (figure 4), we also observed an inverse correlation between serum magnesium (Mg; x axis) and HbA1c (y axis). Out of the three trend lines in Fig. 5 & 6, the order of decline is in the order as follows y=-100x+8.815 (R^2=0.001), y=-0.098x+12.78 (R^2=0.082), and y=-0.018x+2.070 (R^2=0.043). The overall p value demonstrated significant result at p <0.05 between T2DM group subjects and healthy control group subjects when compared the means of FBS, HbA1c, and Mg except that of age.

In the present study pertaining to healthy control group subjects Figure 5, an inverse correlation between age (x axis) with HbA1c (y axis); age (x axis) and Mg (y axis) were established as evident from the graph shown. Out of the two trend lines in Fig. 7, the order of decline is in the order as follows y=-0.01+6.733 (R^2=0.012) and y=-0.033x+3.75 (R^2=0.073).

**Figure 1:** Mean values of Age and FBS in control and T2DM subjects

![Figure 1](image)

**Figure 2:** Mean values of HbA1c and Mg in control and T2DM subjects

![Figure 2](image)
Figure 3: Scatter diagram showing relationships between Age with FBS and Mg in T2DM group

Figure 4: Scatter diagram showing relationships between Mg and HbA1c in T2DM group

Figure 5: Scatter diagram showing relationships between Mg and HbA1c in T2DM group

Discussion
Questions that are asked in this study were to compare the plasma glucose, glycated hemoglobin, and Mg concentrations of patients with T2DM and healthy controls in Bundelkhand region and also to know the association of blood glucose and HbA1c with Mg in respective groups.
The T2DM group subjects showed altered FBS, HbA1c, and Mg when compared with healthy control group subjects. Insignificant difference was observed in the age parameter when compared between the two groups.

In the present study pertaining to T2DM group subjects, an inverse correlation between age and FBS was observed, but not in healthy controls. This finding suggests that increased blood sugar in T2DM group may be caused by increase age in the subjects\cite{33,34}. Literature related to T2DM reveals that T2DM is one of the aging diseases in the present world and our finding also infers the concerns with age in T2DM subjects\cite{35,36}. Studies reported that individuals above 40 years of age are more susceptible to develop T2DM\cite{37,38}. Interesting point is that no correlation was observed in the control group when compared between age and blood sugar, however, we observed insignificant difference in age when compared between T2DM and controls. Keeping in view of this finding, we suggest that individuals, who have predisposition to T2DM, are prominently driven towards the initiation of the disease rather than the individuals who has fewer predispositions. Therefore it is not coincidental to report that older adults have the highest prevalence of diabetes, and such individuals have traditionally not been included in some studies that involve research on diabetes \cite{33,34}.

It is interesting that a correlation between age and HbA1c was negative in the T2DM group and also control group. At first it seems contradictory, but possible explanation could be that the oxidative stress increases with age and increase in HbA1c is compensatory to the increase in age and the free radical production. Many studies have shown that people with T2DM tend to have higher oxidative stress compared to healthy controls compared with same age group individuals\cite{1,3,4}. Though the present did not estimate free radicals but it is evident through the literature that oxidative stress is increased in T2DM patients and also in aged controls\cite{39-40}.

We observed significant lower Mg levels in T2DM group subjects when compared to control group subjects and an inverse correlation between serum Mg and HbA1c in T2DM group. The lower level was due to hyperglycemia present in T2DM subjects. Osmotic diuresis is seen in T2DM subjects, and frequent urination causes loss of Mg as suggested by the studies\cite{41-44}. In addition, re-absorption of Mg in the tubules needs insulin sensitivity, but resistance of the tubules towards insulin because of insulin resistance may hamper the re-absorption of Mg and subsequently Mg is not reabsorbed but excreted in the urine\cite{13,45}. Similar finding has been shown in studies performed with T2DM subjects\cite{13,45}.

The other fact is that free radicals change the oxidation state of the Mg which hinders the bioavailability of the Mg in the body \cite{46-48}. This fact can be explained with the finding of the present study of inverse correlation between age and Mg in the control group. As discussed earlier that free radicals are increased as the age progresses. These free radicals can alter the oxidation state of the minerals and thus lost from the body without getting used. Studies have shown the justification of this fact\cite{7,8}. This could imply that the administration of Mg may be therapeutically beneficial.

**Conclusion**

In conclusion, we observed lower Mg levels in T2DM individuals in the Bundelkhand region. As Mg depletion aggravates insulin resistance and may result in increased loss through urine, it may be advisable to periodically monitor Mg concentrations in T2DM subjects. Moreover, further research is imminent to understand the deeper insights into the association of Mg with T2DM prior to the initiation or after initiation of T2DM.

**Conflict of interest:** None declared.
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