Correlative study of serum magnesium levels & Dyslipidemia in patients with type 2 diabetes mellitus with & without microvascular complication in patients attending M Y Hospital

Dr. P.D.Sarkar, Dr. Bhavana Tiwari, Dr. Sangita Paneri, Dr. Rajeev Lohokare
Professor and HOD, Resident, Professor, Associate Professor
Department of Clinical Biochemistry,
M.G.M. Medical College & M.Y. Hospital Indore (MP) INDIA

*Corresponding Author:
Dr Bhavana Tiwari
Resident, Department of Clinical Biochemistry,
M.G.M. Medical College & M.Y. Hospital Indore (MP) INDIA

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

ABSTRACT
Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia resulting in complications like Retinopathy, Cardiovascular disease, Stroke, Nephropathy, Foot ulcers and Neuropathy. Magnesium has an important role to regulate blood sugar levels and energy metabolism in the body. In order to study role of Magnesium in Diabetes & Diabetes associated complications, present study was carried out in Dept. of Biochemistry MGM Medical College and M.Y. Hospital Indore on 150 patients. 50 healthy subjects as controls & 100 diabetic patients were divided into 50 patients without complication & 50 patients with complications. Fasting blood sample was analyzed for Blood sugar, Magnesium, HbA1C and Lipid profile. In our study we found serum Magnesium levels in patients of DM with complication was very low 1.12 to 1.6 as compared to control group ranging from 2.05 to 2.49 with p value highly significant <0.001. While in patients of DM without complication it was in 1.52 to 2.16 range.

Keywords: Diabetes mellitus, Hyperglycemia, Insulin, Magnesium, Retinopathy

INTRODUCTION
Type 2 diabetes mellitus (T2DM) prevalence in global perspective is over 300 million and in future will rise to over 600 million in next decades. In India 69.2 million people are suffering from diabetes and approximately 98 million people will develop T2DM by the year 2030 (WHO & the International Diabetes Federation Atlas report 2015) Prevalence of diabetes in India is about 8.8%. ICMR studies indicated that out of total diabetic cases, a large proportion of patients were undiagnosed. Diabetes and its complications play a major role to increase the economic burden on country’s health sector due to their significant effect on mortality & morbidity. Studies suggests that patient detected T2DM for the first time must have diabetes for at least 4 to 7 years. Out of total patients with chronic & severe T2DM, complication like retinopathy in 25%, nephropathy in 9% and neuropathy in 8% of patients have been reported.

Magnesium has a very important role in various metabolic reactions, hormone receptor binding, DNA and protein synthesis, nerve-transmission, blood sugar regulation and energy metabolism. It also influences the release and activity of insulin & thus has effect on glucose homeostasis and development of complications like retinopathy, nephropathy and...
neuropathy, So there may be a strong association between T2DM & magnesium levels.

Due to the increasing prevalence of DM in India, the present study was conducted in central part of India with an objective to evaluate the serum magnesium, blood sugar, HbA1c and lipid profile in type-2 diabetes cases with & without complication and to compare them with controls and to explore the association between them & correlate them.

Materials and Methods

The present study was conducted by the Department of Clinical Biochemistry M.G.M. Medical College & M.Y. Hospital Indore after approval from Ethical committee. Written informed consent was obtained from age & sex matched 100 cases of T2DM patients with age group of 45-68 years attending the Diabetic OPD. Fifty age and sex matched apparently healthy individuals with normal plasma glucose & without symptoms of DM were taken as controls.

T2DM patients were diagnosed on the basis of biochemical investigations as per WHO criteria. Confirmed & diagnosed cases of Diabetic retinopathy, Neuropathy & Nephropathy has been chosen for the study. Most commonly accepted classification for Retinopathy is according to International Clinical Diabetic Retinopathy Scale which classifies diabetes retinopathy into Non Proliferative (NPDR) and Proliferative Diabetic Retinopathy (PDR) (WHO, 2005).

Patients with diabetes for 10-15 years, with and without Diabetes associated complication were included in study & Patients other than Diabetes associated complication were excluded from the study.

After an overnight fast, blood samples were collected in Clot activator tubes for estimation of fasting blood glucose, serum Magnesium, HbA1C, & lipid profile. Postprandial blood sugar was measured two hours after a standard meal. Blood glucose was estimated by GOD POD method. HbA1c estimation was done by Immuno turbidimetric method. Calmagite endpoint method was used to estimate Serum Magnesium with normal range between 1.8-2.6 meq/dL. Serum cholesterol, triglyceride were estimated by using commercially available kits. All assays were done on Selectra Pro Automated Analyzer.

Statistical analysis was performed using the IBM SPSS software version 15 and Microsoft excel sheet. Data were expressed as the mean (± SD). The t test, chi-square test were applied to compare the categorical data. The correlation of serum Magnesium levels in control & in Diabetes patients with & without complications was done by Pearson's correlation analysis, p Value (p ≤ .001) was considered significant.

RESULTS

In our study maximum patients of type-2 diabetes mellitus were male (63%). Out of total 50 patients of DM with complications, 62% with retinopathy (non-proliferative) was observed. Serum Magnesium levels (Table-1) in control (Group -1) with mean ± SD of 2.75 ± 0.22 while in patients of DM without complication (Group-2) with mean ± SD of 1.84 ± 0.32 & in patients of DM with retinopathy (Group-3) it was very low with mean ± SD of 1.36 ± 0.24 with highly significant p value < 0.001. Prevalence of hypomagnesemia is markedly raised in patients with Diabetic retinopathy than in patients without retinopathy. Hypomagnesemia in Diabetic patients & in control subjects was respectively 43.5% versus 9.2%.

Fasting blood glucose levels in group-1 was expressed as mean ± SD of 91.70 ± 10.73, in group-2 it was 167.00 ± 13.64 & in group-3 it was 223.44 ± 16.04. Serum Post Prandial blood glucose levels were as mean ± SD (134.20 ± 8.47), (211.70 ± 9.37) & (264.58 ± 13.53) in three different groups respectively (Table-1).

HbA1c levels in three group were (4.64 ± 0.33), (7.51 ± 0.53) & (10.58 ± 2.4) respectively with significant p value < 0.001.

Serum cholesterol levels in the groups were mean ± SD of (159.27 ± 14.62), (216.43 ± 15.48) and (274.34 ± 12.58) & Serum Triglyceride levels as mean ± SD of (121.75 ± 8.29), (156.15 ± 6.53) and (179.32 ± 11.36) in all the three groups, which was significant (p value < 0.001) statistically.

Our study has revealed that Magnesium deficiency was profoundly evident (Graph-2) in T2DM patients with microvascular complications with mean ± SD (1.36 ± 0.24) compared to T2DM without microvascular complications (1.84 ± 0.32) and (2.75 ± 0.22) in controls.
Significantly raised serum cholesterol, triglyceride & HbA1C levels were observed in Diabetes with and without complication than in controls. (Graph -1)

Serum Magnesium has inverse correlation with blood sugar, HbA1C & lipid profile levels.

**TABLE 1 - Serum concentration of various Biomarkers in Control & Cases**

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>Normal healthy control (N=50)</th>
<th>Diabetes without complication (N=50)</th>
<th>Diabetes with complication (N=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP-1</td>
<td>GROUP-2</td>
<td>GROUP-3</td>
<td></td>
</tr>
<tr>
<td>MAGNESIUM</td>
<td>2.75 ± 0.22</td>
<td>1.84 ± 0.32</td>
<td>1.36 ± 0.24</td>
</tr>
<tr>
<td>CHOLESTEROL</td>
<td>159.27 ± 14.62</td>
<td>216.43 ± 15.48</td>
<td>274.34 ± 12.58</td>
</tr>
<tr>
<td>TRIGLYCERIDE</td>
<td>121.75 ± 8.29</td>
<td>156.15 ± 6.53</td>
<td>179.32 ± 11.36</td>
</tr>
<tr>
<td>FBS</td>
<td>91.70 ± 10.73</td>
<td>167.00 ± 13.64</td>
<td>223.44 ± 16.04</td>
</tr>
<tr>
<td>PPBS</td>
<td>134.20 ± 8.47</td>
<td>211.70 ± 9.37</td>
<td>264.58 ± 13.53</td>
</tr>
<tr>
<td>HbA1C</td>
<td>4.64 ± 0.33</td>
<td>7.51 ± 0.53</td>
<td>10.58 ± 2.4</td>
</tr>
</tbody>
</table>

**GRAPH- 1 Comparison of Biochemical parameters between Control & Diabetes Patients without complication and with complications**

**GRAPH- 2 Comparison of serum Magnesium between Control & Diabetes Patients**
DISCUSSION

Mg2+ is an essential ion has an important role in glucose & energy homeostasis, protein synthesis and stability of DNA\cite{12}. Due to its important regulatory role, its serum levels are tightly regulated between 1.8–2.6 meq/dL in healthy individual. Chaudhary DP et, al. in their study shown an inverse relationship between dietary Mg2+ intake and risk of developing T2DM \cite{13-15}. The hypomagnesemia prevalence in T2DM ranges between 14 to 48% as compared to healthy subjects in which it is between 2.5 to 15%\cite{16}. Guerrero-Romero F, Rodríguez-Morán M et, al. in their study stated the beneficial effects of Mg2+ supplementation on glucose metabolism and insulin sensitivity\cite{17-19}. In our study hypomagnesemia is more prevalent in male patients which is similar with the results of Ghaour et, al\cite{20}. However, Kahn et, al. found a higher incidence of Diabetic retinopathy in females\cite{21}.

Magnesium on binding with tyrosine residues, which on auto phosphorylation cause activation of cell signalling pathway and it also increases the affinity of the insulin receptor for ATP thus it regulates insulin sensitivity\cite{22-24}. In T2DM patients the main mechanism of insulin resistance due to low magnesium is because of defective or reduced receptor phosphorylation. According to Humphries S. et, al. Lima M. et, al. & Nadler JL et, al. increased insulin resistance in T2DM patients are associated with hypomagnesaemia\cite{25-27}.

Obesity is also a risk factor to develop T2DM in which adipocytes generate proinflammatory mediators like interleukin-1 and tumour necrosis factor-α to produce reactive oxygen species\cite{28}. Mg2+ has an anti-inflammatory action and in obese patients low Mg2+ levels develops an inflammatory environment.

Mg2+ deficiency causes insulin resistance by neutrophil activation and oxidative stress\cite{29-31}. In hyperglycemia increased urinary Mg2+ excretion & reduced reabsorption of Mg2+ contributes to hypomagnesemia\cite{32,33,11}. Sodium potassium ATPase activity which is responsible for maintenance of sodium, potassium and glucose transport across the membranes is altered by Mg2+ deficiency.

The exact mechanism for microvascular complication in T2DM is not clear till now however, Saproo N et, al. mentioned that low Mg2+ levels has inhibitory action on prostacyclin receptors causing an imbalance between prostacyclin and thromboxane effect which induces atherogenesis and later on develop microvascular complications\cite{6}. Grafton G. et, al. concluded in their study that as mean Mg2+ level decreases, severity of retinopathy increases\cite{34}. Out of several probable causes of reduced Mg2+ level in T2DM, exact cause of Diabetic hypomagnesemia is still unknown.

Our study has shown that out of total 50 cases with complications, 62% of patients had retinopathy (all non-proliferative), 22% had nephropathy & 16% had neuropathy, which is similar to studies by Gurjar P. et, al. and Kaur P. et, al. that shows the association of hypomagnesemia with Diabetic retinopathy\cite{35,36}. the percentage of hypomagnesemia was higher in the Diabetic patients than in control subjects by four times (43.5% versus 9.2%) which was significantly high statistically (p < 0.001). Our results correlate with study by Chauhan KP et,al. and Mohanty SS et,al. which has mentioned it from 47.7%,versus 13.5%\cite{37-39}.

CONCLUSION

The present study concluded that reduced Magnesium levels was found in cases of T2DM without complications and significantly decreased in patients with retinopathy than in controls. Serum cholesterol & triglyceride levels are found raised in the patients of T2DM without complication & it is significantly increased in patients with complications as compared to control Subjects. An inverse correlation is found between Mg2+ level & lipid profile in patients of T2DM with & without complications.

Hypomagnesaemia in patients with T2DM is frequently overlooked and undertreated. A multidisciplinary approach is usually applied for the treatment of T2DM patients so that every potential complicating factor must be closely monitored and treated.

In summary, Mg deficiencies in T2DM patient can be corrected by supplementing oral Magnesium which is useful to improve insulin sensitivity there by reducing the fasting and postprandial glucose levels and also have a significant effect on oxidative stress and systemic inflammation. Larger prospective
studies are needed to support the potential role of dietary Mg supplementation in type 2 diabetes patients.

ACKNOWLEDGEMENTS: We would like to express our gratitude to the hospital laboratory staff, for their unconditional support during sample collection & processing. We also want to thank all the study participants for their willingness to participate in this study.

REFERENCES

21. Hubbard SR. Crystal structure of the activated insulin receptor tyrosine kinase in complex