Abstract
Introduction: Magnesium which is present in the extra-cellular compartment is very vital for antagonising calcium physiology. Hypomagnesemia is sensed as a stressor by our body suggesting that magnesium metabolism plays an essential role in the evolving of metabolic syndrome. Statistical data on the association of hypomagnesemia with metabolic syndrome would help the clinicians to overcome therapeutic compliance of the patients, so our study was designed to estimate the levels of serum magnesium in patients with metabolic syndrome and healthy controls and to correlate it with the components of metabolic syndrome.

Materials and Methods: The present case-control study was conducted in patients with metabolic syndrome attending a tertiary care hospital in Kanchipuram District during the period from April to December 2017. 65 patients of metabolic syndrome & 65 controls who attended the various out-patient departments of the hospital were selected for the study. Waist circumference, blood pressure, fasting plasma glucose, serum triglycerides, HDL-cholesterol and serum magnesium was estimated, compared and analyzed.

Results: This study has proven that the mean serum magnesium level in patients with metabolic syndrome was 1.3±0.07mg/dL while in controls it was 2.06±0.26mg/dL. A highly significant difference (p<0.00001) was observed between the cases and controls. Serum magnesium levels ranged between 1.25 to 1.49 mg/dL in cases and 1.7 to 2.5 mg/dL in controls, thus making it evident that there is a strong association between hypomagnesemia and metabolic syndrome.

Conclusion: The study has made the association of hypomagnesemia and metabolic syndrome evident. Further studies with larger sample size will help in providing data to implement supplementation of oral magnesium for effective correction of metabolic derangements observed in metabolic syndrome.

Keywords: Hypomagnesemia, Metabolic syndrome.
Exclusion Criteria
1. Coexistence of less than 3/5 components mentioned in the inclusion criteria for MS (Eg: A confirmed case of only diabetes mellitus or only hypertension)
2. Known cases of renal failure
3. Acute or chronic diarrhoea/ malabsorption state
4. Magnesium/ multimineral supplement intake
5. Recent intake of drugs that alter magnesium metabolism like diuretics, anti-biotics and antacids.
6. Recent metabolic acidosis or sepsis
7. Pregnancy & lactation

Informed consent for participation was obtained from the participants. A semi-structured proforma was used for obtaining relevant personal data. Parameters like systemic blood pressure and anthropometric measurements like waist circumference were recorded according to the standard guidelines. 5mL of fasting (8-10hours) blood sample for analysis was collected. Serum triglycerides and HDL-cholesterol was analysed. 2mL of blood was aliquoted for magnesium analysis. Another 2mL of blood was aliquoted into sodium fluoride – potassium oxalate tube for plasma fasting glucose estimation. They were centrifuged at 3000rpm for 20minutes. All the analytes were estimated using Biosystems BA200 fully automated analyser. Serum triglycerides, HDL –cholesterol, fasting plasma glucose, magnesium were estimated by glycerol phosphate oxidase, direct method, glucose oxidase- peroxidase, xylidyl blue method respectively.

Statistical Analysis
All the results obtained were statistically analyzed using SPSS software 17.0v. Mean & standard deviation were found for all parameters. “t” test was used to compare the means of the two groups, significance level was kept at 5%. Correlation coefficient was done using Pearson’s method to compare serum magnesium levels with fasting plasma glucose, serum triglycerides, HDL-cholesterol, systolic blood pressure, diastolic blood pressure and waist circumference.

Results
In this study 37 males and 28 females were having metabolic syndrome and the rest 32 males and 33 females were controls. The age group of the patients with metabolic syndrome in this study was 35-60 years.

All the study subjects were screened for the components of metabolic syndrome (Table 1). The fasting plasma glucose among metabolic syndrome patients was in the range of 112-436mg/dL with the mean, standard deviation 180.2±58.9mg/dL.

The following parameters like fasting plasma glucose, serum triglycerides, serum HDL-Cholesterol, systolic blood pressure and diastolic blood pressure were significantly higher with the p value <0.00001, while the waist circumference had an p value of 0.002 in patients with metabolic syndrome when compared with the controls.

The serum magnesium level (Fig. 1) among patients with metabolic syndrome and controls was significantly different (p value <0.00001) with the cases having a mean value of 1.36mg/dL, while in controls the mean value was 2.06mg/dL. All the components of metabolic syndrome were looked for Pearson’s correlation coefficient (Table 2). Strong positive correlation (r = 0.76) was found between serum magnesium and HDL-cholesterol, while there was a negative correlation between serum magnesium and triglyceride (r = -0.78). The same was observed with systolic blood pressure also (r = -0.77). Moderate level of negative correlation was observed between magnesium and fasting plasma glucose and diastolic blood pressure. Magnesium levels and waist circumference had very low levels of negative correlation. The values were also plotted on scatter plot for Pearson’s correlation coefficient between serum magnesium with triglycerides, HDL- cholesterol, systolic blood pressure respectively (Fig. 2-4).

### Table 1: Components of Metabolic Syndrome - comparison among patients with metabolic syndrome and controls

<table>
<thead>
<tr>
<th>Variables</th>
<th>Metabolic syndrome patients (n=65)</th>
<th>Controls (n=65)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose (FPG in mg/dL)</td>
<td>180.2±58.9 112-436</td>
<td>90.3±61 77.4-99.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Serum triglycerides (TGL in mg/dL)</td>
<td>176.3±21.7 160-220</td>
<td>92.8±15.1 70-134</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Serum HDL-Cholesterol (HDL-C in mg/dL)</td>
<td>40.8±8.6 23-62</td>
<td>60.8±3.6 54-68</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic Blood Pressure (SBP in mmHg)</td>
<td>146.1±7.5 134-158</td>
<td>124.8±3.9 120-134</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (DBP in mmHg)</td>
<td>88.3±4.3 80-96</td>
<td>82.8±2.5 80-88</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist Circumference (WC in cm)</td>
<td>113.0±6.9 102-126</td>
<td>108.7±5.7 100-122</td>
<td>0.002</td>
</tr>
</tbody>
</table>

### Table 2: Pearson’s Correlation Co-efficient for serum magnesium and parameters of metabolic syndrome

<table>
<thead>
<tr>
<th>Variable 1</th>
<th>Variable 2</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose</td>
<td>Serum Magnesium</td>
<td>-0.65</td>
</tr>
<tr>
<td>Serum triglycerides</td>
<td>Serum Magnesium</td>
<td>-0.78</td>
</tr>
<tr>
<td>Serum HDL-Cholesterol</td>
<td>Serum Magnesium</td>
<td>0.76</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>Serum Magnesium</td>
<td>-0.77</td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td>Serum Magnesium</td>
<td>-0.55</td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>Serum Magnesium</td>
<td>-0.28</td>
</tr>
</tbody>
</table>
Fig. 1: Comparison of serum magnesium levels among patients with metabolic syndrome and controls

Fig. 2: Scatter plot of serum magnesium and triglyceride

Fig. 3: Scatter plot of serum magnesium and HDL – C
Discussion

In study showed that the cases and controls were aged between 36-60 years. Of all the study subjects males and females were equally distributed, i.e., 50%. All the cases had statistically significant difference of serum magnesium levels, fasting plasma glucose, serum triglycerides, HDL-Cholesterol, systolic blood pressure, diastolic blood pressure and waist circumference when compared with the controls.

Previous studies were also reporting that mean serum magnesium was significantly decreased in patients with metabolic syndrome when compared with the healthy adults. Correlation analysis observed a negative correlation that was significant, between serum magnesium levels and fasting blood sugar, systolic, diastolic blood pressure, serum triglyceride. A positive correlation was observed between serum magnesium and serum high-density lipoprotein levels.

Magnesium has an important role in glucose mediated insulin release from the beta cells of pancreas through its effect on cellular calcium homeostasis. Low intracellular Mg concentrations, following hypomagnesemia affects the tyrosine-kinase activity of insulin receptor causing an increased intracellular calcium concentration. An inverse relationship between serum magnesium, fasting blood glucose and HbA1C was also observed in previous studies.

Thus, hypomagnesemia is implicated in insulin resistance causing type 2 diabetes mellitus, hypertension and cardiovascular disease. Rosolova et al has shown an inverse association between plasma magnesium and fasting insulin levels in study subjects with diabetes mellitus and apparently healthy individuals. It is also proven that hypomagnesemia is significantly associated with poor glycemic control.

Extra-cellular magnesium acts as a physiological calcium antagonist. Anti-hypertensive effect of serum magnesium is executed by inhibiting intracellular calcium mobilization, improving the myocardial contractility by reducing the pre-load to the heart and producing vasodilation in all blood vessels. It is observed that there is an association between low serum magnesium levels and the risk of developing hypertension among rural population in North India.

Several rate limiting enzymes important in the metabolism of lipids are influenced by serum magnesium levels. Normal serum magnesium level has an inhibitory control over 3-hydroxy-3-methylglutaryl coenzyme A reductase and increases lipoprotein lipase activity. This in turn prevents higher serum cholesterol and triglyceride levels. Guerrero-Romero et al observed hypomagnesemia to be independently related to dyslipidemia in Mexican population.

Emerging evidence indicates that a high intake of magnesium from diet or supplements can affect favorably in reversing the metabolic abnormalities observed in metabolic syndrome and can be an effective mode of treatment for metabolic syndrome.

This study has proven that the mean serum magnesium level in patients with metabolic syndrome was 1.3±0.07mg/dL while in controls it was 2.06±0.26mg/dL. A highly significant difference (p <0.00001) was observed between the cases and controls. Serum magnesium levels ranged between 1.25 to 1.49 mg/dL in cases and 1.7 to 2.5 mg/dL in controls, thus making it evident that there is a strong association between hypomagnesemia and metabolic syndrome.
Conclusion
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References

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