Original Article

Association of Serum Magnesium with Plasma Glucose Level in Gestational Diabetes Mellitus

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Abstract:
Background: *Magnesium (Mg) is the fourth most abundant mineral in the body. It acts as an essential co-factor for enzymes especially those involved in phosphate transfer reactions and plays important role in phosphorylation of tyrosine kinase of insulin receptor. Low serum Mg is a strong predictor of the development of diabetes by impairing the action of insulin. Diabetes Mellitus (DM) is characterized by hyperglycemia due to absolute or relative deficiency of insulin. Gestational Diabetes Mellitus (GDM) is a form of hyperglycemia developed first ever during pregnancy. Clinical detection of GDM is carried out to identify pregnancy at increased risk for perinatal morbidity and mortality. This study showed that decrease level of serum Mg had inverse correlation with increased level of plasma glucose in GDM.* ***Methodology:*** *This was a cross sectional study of serum Mg in GDM patients was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka for a period of 1 year. Total fifty subjects were recruited in this study; among them thirty women with GDM were selected as case (Group-I) and twenty non pregnant healthy women were taken as control (Group- II). GDM patients diagnosed by OGTT according to WHO criteria and subsequently measurement of serum Mg level was performed in both group.* ***Results:*** *Mean serum Mg concentration of GDM patients and non-pregnant healthy women value was 0.71±0.10 mmol/L and 0.82±0.10 mmol/L respectively. Mean serum concentration of Mg was inversely correlated with mean fasting plasma glucose (8.3 mmol/L) when 'r' value was -0.577 at p<0.05 level in GDM cases.* ***Conclusion:*** *Decreased serum Mg might be the cause of increased plasma glucose level in GDM cases. So, Mg supplement in pregnant women can play a role in preventing GDM.*

Key words: DM, Gestational Diabetes Mellitus (GDM), Magnesium (Mg)

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Introduction:
Diabetes mellitus (DM) is a common multisystem endocrine and metabolic disorder, which is a leading cause of mortality and morbidity globally. Diabetes is characterized by hyperglycemia due to absolute or relative deficiency of insulin. Lack of insulin affects the metabolism of carbohydrate, protein, fat, water and electrolytes[1].

Gestational Diabetes Mellitus (GDM) is a form of hyperglycemia developed first ever during pregnancy. Clinical detection of GDM is carried out to identify pregnancy at increased risk for perinatal morbidity and mortality. GDM complicates roughly about 1-14% of pregnancies. There is a greater risk of developing recurrent GDM in subsequent pregnancy. The prevalence rate of GDM is 4.8 to 7.5% among rural Bangladeshi women[2]. Whatever be the etiology, in all cases, the hyperglycemia of DM develops because of an absolute or relative deficiency of insulin. Insulin exerts its function by three distinct mechanisms. Mechanisms are i) insulin receptor mediated signal transduction ii) glucose transport across the cell membrane and iii) induction of enzyme synthesis. For performing action, insulin binds with specific insulin receptor in the cell membrane of the most tissue.

Magnesium is the fourth most abundant mineral in the body. It acts as an essential co-factor for enzymes especially those involved in phosphate transfer reactions and concerned with cell respiration, glycolysis and trans-membrane transport of other cations such as calcium and sodium[3,4]. Normal Serum Mg range is between 0.7-1.05 mmo1/L. It activates phosphorylation of tyrosine kinase of insulin receptor[5-7]. Walti *et al.* explains that magnesium depletion appears to have a negative impact on glucose homeostasis and insulin sensitivity[8]. Low serum Mg is a strong independent predictor of the development of diabetes. Thus the impairment of insulin sensitivity

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seems to be related to defective tyrosine activity of the insulin receptor. They explained that since there were several enzymes involved in glucose metabolism that required high-energy phosphate bonds, Mg, as a cofactor is required.

Catalano *et al.* found that women with GDM have significantly lower level of serum Mg in comparison with healthy women[9]. So there may have some association between low serum Mg level and development of GDM. The exact reason for decreased Mg concentration in GDM is not clear but increased need and an increase in the renal clearance of Mg during pregnancy can aggravate the deficiency leading to GDM. Due to modern dietary habits and ignorance, pregnant women may have magnesium deficiency before pregnancy.

Plasma glucose concentration was decreased following Mg administration to diabetic subjects and showed a significant increase in percent insulin sensitivity. So, Magnesium supplementation has a beneficial effect on insulin action and glucose metabolism[10,11]. Butte NF state that GDM is heterogeneous disorder in which age, obesity, and genetic backgrounds contribute to the severity of the disease[12]. It is the common metabolic abnormalities occurring during pregnancy and incidence rate of GDM is 9.2% in Asia[13]. In long term follow-up studies, recently reviewed by many researcher revealed that most, but not all women with GDM do progress to diabetes after pregnancy. Thus GDM provides a unique opportunity to study the early pathogenesis of diabetes and to develop interventions to prevent the diseases[14]. For the above mentioned reasons the present study was designed to observe the real association between serum Mg level with plasma glucose level in GDM cases. So that special attention can be given to this group of women during pregnancy for prevention of the pregnancy adverse outcomes.

Materials & Methods:

This cross sectional study was carried out in the Department of Biochemistry, Dhaka Medical College (DMC), Dhaka for a period of one year. Sample population were selected by brief history and on the basis of inclusion and exclusion criteria. Inclusion criteria for GDM case were age (25-35 years), 2nd & 3rd trimester of pregnancy and GDM patients not receiving anti-diabetic drug therapy. Inclusion criteria for control were Non pregnant healthy women (Age matched). Exclusion criteria were history of DM before pregnancy, Hypertension, Preeclampsia, Diuretic therapy and Obesity (Subjects having BMI more than 27.3 kg/m^2 was excluded from the study).

GDM patients diagnosed as diabetic by OGTT according to WHO criteria were recruited from gynecology and obstetrics outpatient department of BIRDEM. Serum Mg of GDM cases were measured and compared with serum Mg of non-pregnant healthy control. Permission for the study was taken from Ethical Review Board of DMC.

Data were collected through a preformed data collection sheet (questionnaire). BMI was calculated by the recorded weight during first antenatal check-up of 1st trimester. Blood samples taken from pregnant women during OGTT were used for this study. Plasma glucose was measured by enzymatic colorimetric method. Serum was analyzed for magnesium by colorimetric method using vitros Mg slides. Informed written consent was taken from study subjects. Data were analyzed using SPSS software and MS Excel. Mean values of serum Mg of two groups were compared by unpaired 't' test. Correlation was assessed by using Pearson's correlation coefficient test. P-value <0.05 was considered as significant.

Results:

Out of total 50 women 30 were GDM as case (Group-I) and 20 were non pregnant healthy women as control (Group- II).

Table-I: Baseline clinico-biochemical characteristics of study subjects (n=50)

Characteristics	Group I (GDM) n=30	Group II (Non pregnant healthy women) n=20
Age (years)	29.9±2.6	29.6± 2.7
Gestational age (Weeks)	26.3±5.8	-
Fasting plasma glucose level (mmol/L)	8.3±0.34	4.2±1.41

All results were expressed as their mean values ± SD (Standard deviation). Age (in yrs) of GDM cases &non pregnant healthy women control group were 29.9 ± 2.6& 29.6 ± 2.7 respectively. Gestational age (weeks) of GDM was 26.3± 5.8. Fasting plasma glucose of group I& group II were 8.3 ± 0.34, 4.2 ± 1.41mmol/L respectively as shown in Table- 1.

Table-II: Comparison of serum Mg concentration between group 1 and group II

Parameter	Group I (GDM) n=30	Group II (Non Pregnant healthy women) n=20	p value
Serum Mg (mmol/L)	0.71 ± 0.10	0.82 ± 0.10	<0.001*

Unpaired 't' test done * Highly significant

Figure-1 showed statistically significant correlation of serum Mg with fasting plasma glucose level in GDM cases where mean serum concentration of Mg (0.71 mmol/L) was inversely correlated with mean plasma glucose (8.3 mmol/L) when 'r' value was -0.577 at $p<0.05$ level.

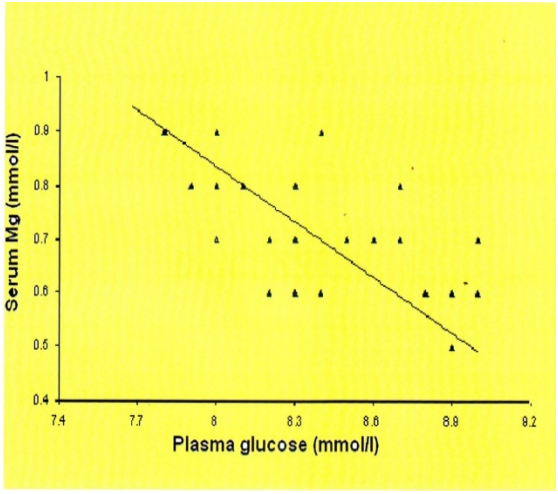

Figure-1: Correlation of serum Mg with fasting plasma glucose level in GDM cases.

Discussion:

In this study, we estimated the serum Mg level in GDM cases and non-pregnant healthy women as control to investigate the association of serum magnesium (Mg) with GDM. Mg mainly present inside the cell but serum Mg measurement is the most readily available and widely used test of Mg status. The present study has revealed the mean serum Mg concentration is 0.82 ± 0.10 mmol/L in healthy control women. This is nearly consistent with several other studies[15,16]. Mean serum Mg concentration found in GDM was 0.71 ± 0.10 mmol/L and in non-pregnant healthy women mean was 0.82 ± 0.10 mmol/L. GDM patients of this study have shown serum Mg concentration significantly low in comparison to control group. Same phenomenon was observed in other study[17,18].

The reasons why low Mg is common in GDM patients are not clear but may include lower dietary intake, increase demand during pregnancy, increase urinary loss, impaired absorption and treatment with diuretics[19]. Mg depletion has a negative impact on glucose homeostasis and plays a role in development of diabetes mellitus as well as on the evolution of complication such as retinopathy, thrombosis and hypertension[20]. Low serum Mg is the common finding of GDM and decreased insulin sensitivity or insulin resistance (IR) is the underlying pathophysiology of GDM. IR means, in its simplest sense, that the ability of insulin to disposal of glucose in the liver, skeletal muscle and other peripheral tissues is compromised[21,22].

Magnesium is one of the most abundant intracellular divalent cation. It is a cofactor of many enzymes involve in glucose metabolism as it is involve in phosphorylation and is a co factor for ATPase and adenylate cyclase enzymes. It is required for both proper glucose utilization and insulin signaling. The suppressed magnesium concentration may result in defective tyrosine kinase activity and modify insulin sensitivity by influencing receptor activity after binding or by influencing intracellular signaling and processing.

Magnesium deficiency may affect the development of insulin resistance and alter the glucose entry into the cell and metabolic alternations in cellular Mg, which may play the role of a second messenger for insulin action, contribute to insulin resistance[23]. Several studies showed that though diabetes can induce decreased serum Mg but Mg deficiency can also be a risk factor for GDM[24,25]. Our study showed that serum Mg is inversely correlated with plasma glucose level ($r = -0.577$, $p=0.05$) in GDM cases. This study finding is supported by the other studies[25,26]. Reports of some studies however pointed out some doubts regarding the association between serum Mg & glucose metabolism. They found low Mg in diabetes but failed to show significant correlation between these[27]. A number of prospective study suggested that diet supplementation with Mg significantly reduces risk of diabetes and its complication by improving insulin sensitivity[28,29]. No such trial could be done in the present study. Because of time limitation and fund constriction this study failed to trial the effect of Mg supplementation in reversing GDM by decreasing blood glucose level. In future this can be carried out to make the present finding more comprehensive and convincing.

Conclusion:

GDM is one of the most common conditions during pregnancy and its prevalence is increasing in Bangladesh. There are some well-established risk factors for the development of GDM. Decreased serum magnesium has recently been claimed as a risk factor for it. Mean serum Mg concentration in GDM patients was found to be significantly lower in comparison to non-pregnant healthy control women. The results of the present study demonstrated a relationship between decreased serum Mg and development of GDM. It may be prudent in clinical practice to periodically measure serum Mg concentration during pregnancy. If serum Mg is low, an intervention to increase serum Mg can be taken.

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