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ASSOCIATION OF MATERNAL SERUM MAGNESIUM LEVEL WITH GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Gestational diabetes mellitus (GDM) is a common medical disorder of pregnancy, associated with an increased risk of poor maternal and fetal outcome. So the current study was done to find out the association of low serum magnesium levels with GDM. This was a case-control study among purposively selected pregnant women matched for age and gestational age attending the inpatient and outpatient department of Obstetrics and Gynecology, Institute of Child and Mother Health (ICMH), Matuail, Dhaka, from September 2020 to August 2021. A total of 92 singleton pregnant women between 18-35 years of age were included in this study in their 24-40 weeks of gestation. Among them, 46 diagnosed women with GDM were considered the cases, and the rest of the 46 matched healthy pregnant women were selected as controls. Their serum magnesium level was measured in the laboratory of the Department of Biochemistry in BSMMU, Dhaka. Descriptive analysis was done using the analytic software SPSS v27.0, where required. The overall average serum magnesium levels in both the cases and controls were 1.57±0.28 mg/dL and 1.79±0.33 mg/dL, respectively. Considering serum magnesium level of 1.7 mg/dL as a cut-off value, odd's ratio calculation showed GDM incidence was 3.22 times more likely in pregnant women with low serum magnesium level (<1.7) than those with ≥1.7 mg/dL (OR=3.215; 95% CI=1.368-7.557). There was significant negative correlation of serum magnesium level with both fasting blood sugar level (r=-0.215, p=0.039) and 2hrs after 75g glucose level (r= -0.348, p=0.001). In conclusion a low level of serum magnesium was found strongly associated with GDM.

KEYWORDS: GDM, serum magnesium (Mg) level.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a metabolic disorder that contributed to adverse pregnancy outcomes and detrimental clinical consequences in both mother and fetus. It is a condition of glucose intolerance with onset or first recognition in pregnancy that is not overt diabetes.[1]

Intracellular magnesium contributes in the regulation of the effects of insulin and glucose uptake; its deficits strongly associated with hyperglycemia, hypertriglyceridemia, insulin resistance (IR) and overproduction of contra-insulin hormones (epinephrine and cortisol)[2] In the liver, Mg^{2+} is an important regulator of enzymes in gluconeogenesis, including glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxy kinase (PEPCK). Hormones such as insulin, glucagon, glucocorticoids and epinephrine influence the key enzyme activities of gluconeogenic enzymes, and Mg^{2+} plays a role in the secretion of all these hormones.[3]

Defective insulin receptor phosphorylation is therefore regarded as the main mechanism by which hypomagnesaemia contributes to insulin resistance in diabetes patients.[4]

A study demonstrated that magnesium is an effective and an underlying factor in identification of disrupted glucose metabolism in pregnant women with gestational diabetes mellitus[5]. But in contrary some study results presented that there was no significant difference between healthy pregnant women and women with GDM in respect to serum Mg concentration.[6,7] Therefore, the previous study results were conflicting and were

performed in a different socio-cultural context.

So, this study was conducted to demonstrate the association of maternal serum magnesium level with gestational diabetes mellitus.

METHODS

This Case control study was conducted in the Department of Obstetrics and Gynecology of the Institute of Child and Mother Health (ICMH), Matuail, Dhaka, from September 2020 to August 2021.Sample size was calculated using method suggested by Sakpal, 2010.[8] A total of 92 pregnant women between 24 to 40 weeks of gestation attending the inpatient and outpatient department of Obstetrics and Gynecology of ICMH, were enrolled in this study. Among them, 46 diagnosd women with GDM according to criteria WHO, 2013,[9] considered the cases and the rest of the 46 matched healthy pregnant women were selected as controls. Criteria for exclusion were pre-gestational diabetes, previous history of GDM, family history of type-2 DM, diagnosed case of chronic renal disease, thyroid disease, chronic hypertension, preeclampsia. After taking informed consent and matching eligibility criteria data were collected from patients using the predesigned structured questionnaire. Serum magnesium level was measured in the department of biochemistry and molecular biology, BSMMU. For this study purpose serum magnesium level 1.7mg/dl was taken as cutoff value, below which level it was considered as a risk for developing GDM; as taken De las Penas et al.,2014.[10] Data were analyzed using SPSS (version 27.0) and presented as table. P-value < 0.05 was considered significant.

RESULTS

In this study purpose respondent's age were matched according to selection criteria and there were no statistically significant difference in between the case and control groups regarding their educational qualifications, occupation and monthly family income (p > 0.05) (Table-I).

Table I: Distribution of the respondents according to their socio-demographic characteristics by group (n=92).

Socio-demographic variables	Group		*p*-value
	Case (N = 46)	Control (N = 46)	
Age (in years)			
18-20	7 (15.2)	7 (15.2)	0.854[a]
21-29	30 (65.2)	32 (69.6)	
30-35	9 (19.6)	7 (15.2)	
Mean ± SD	26.09 ± 5.05	25.89 ± 4.85	0.850[b]
Education qualification			
Up to primary	19 (41.3)	18 (39.1)	0.902[a]
S.S.C.	14 (30.4)	13 (28.3)	
H.S.C. and above	13 (28.3)	15 (32.6)	
Occupation			
House wife	31 (67.4)	28 (60.9)	0.772[a]
Student	4 (8.7)	6 (13.0)	
Garments worker	8 (17.4)	7 (15.2)	
Other service holder	3 (6.5)	5 (10.9)	
Monthly family Income			
< 10,000 Tk	3 (6.5)	1 (2.2)	
10,000 – 25,000 Tk	37 (80.4)	36 (78.3)	0.502[c]
> 25,000 Tk	6 (13.0)	9 (19.6)	

[a]Chi square test was done to measure the level of significance.
[b]Unpaired-t test was done to measure the level of significance.
[c]Fisher's exact test was done to measure the level of significance.
Figure within parentheses indicates percentage.

Case: Pregnant women with GDM.
Control: Healthy pregnant women.

Table II: Distribution of the respondents according to obstetrical characteristics by group (n=92).

Obstetrical characteristics	Case (N = 46)	Control (N = 46)	*p*-value
Trimester of pregnancy			
Second trimester	9 (19.6)	5 (10.9)	0.246[a]
Third trimester	37 (80.4)	41 (89.1)	
Gravida			
Primigravida	17 (37.0)	19 (41.3)	0.669[a]
Multigravida	29 (63.0)	27 (58.7)	
Gestational age (in weeks)			
Mean (±SD) gestational age	32.22 ± 5.07	32.04 ± 4.56	0.863[b]

[a]Chi square test was done to measure the level of significance.
[b]Unpaired t test was done to measure the level of significance.
Figure within parentheses indicates in percentage.

Case: Pregnant women with GDM.
Control: Healthy pregnant women.

On evaluation of the obstetrics characteristics, the distribution of the respondents were found statistically not significant (p>0.05).

Table III: Distribution of mean (±SD) maternal magnesium level by group (case = 46, control = 46).

Parameter	Case (Mean±SD)	Control (Mean±SD)	*p*-value
Serum magnesium level (mg/dL)	1.57 ± 0.28	1.79 ± 0.33	0.001[b]

[b]Unpaired t test was done to measure the level of significance.

Case: Pregnant women with GDM
Control: Healthy pregnant women

Table III demonstrates the distribution of study subjects according to their mean (±SD) serum magnesium level. Here, the mean magnesium levels for case and control group of respondents were 1.57±0.28 mg/dL and 1.79±0.33 mg/dL, respectively. The mean difference of serum magnesium between the two groups was statistically significant (p=0.001).

Table IV: Odds ratios (OR) and 95% confidence intervals (CI) for GDM according to serum magnesium level in pregnancy (Case = 46, Control = 46).

Magnesium (mg/dL)	Groups		p-value	Odds Ratio (95% CI)
	Case N (%)	Control N (%)		
< 1.7	28 (60.9)	15 (32.6)	0.007[a]	3.215 (1.368-7.557)
≥ 1.7	18 (39.1)	31 (67.4)		

[a]Chi-square test was done to measure the level of significance.
Figure within parenthesis indicates in percentage.
CI = Confidence Interval

Case: Pregnant women with GDM
Control: Healthy pregnant women

There was significant difference in regards of serum magnesium level in between case and control groups (p=0.007) and the respondents with serum magnesium <1.7 mg/dL had 3.22 times more chance to develop GDM compared to that of the healthy controls (OR=3.215; 95% CI=1.368-7.557).

Correlation between maternal serum magnesium level and blood sugar

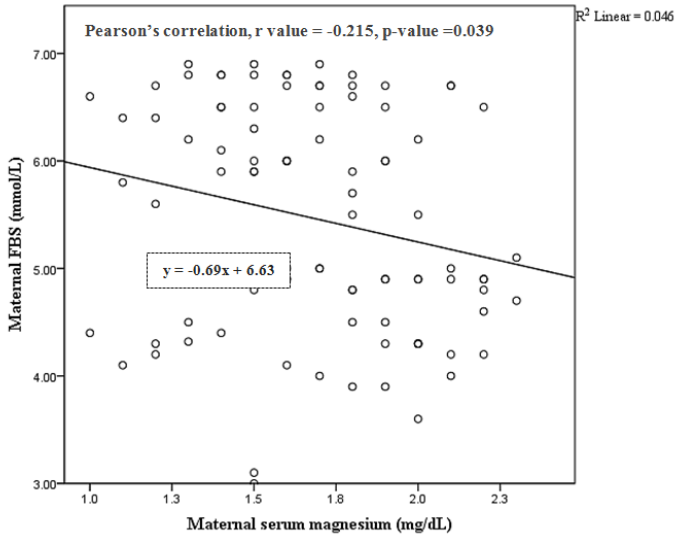

Figure I: Scatterplot diagram showing correlation between maternal serum magnesium level and fasting blood sugar (r= -0.215, p=0.039).

R^2 = percentage of variability of FBS in GDM due to low serum magnesium level and vice versa
r = Pearson's correlation coefficient

Correlation between maternal serum magnesium level and fasting blood sugar is shown in figure I, where significant inverse correlation was observed (r= -0.215, p=0.039).

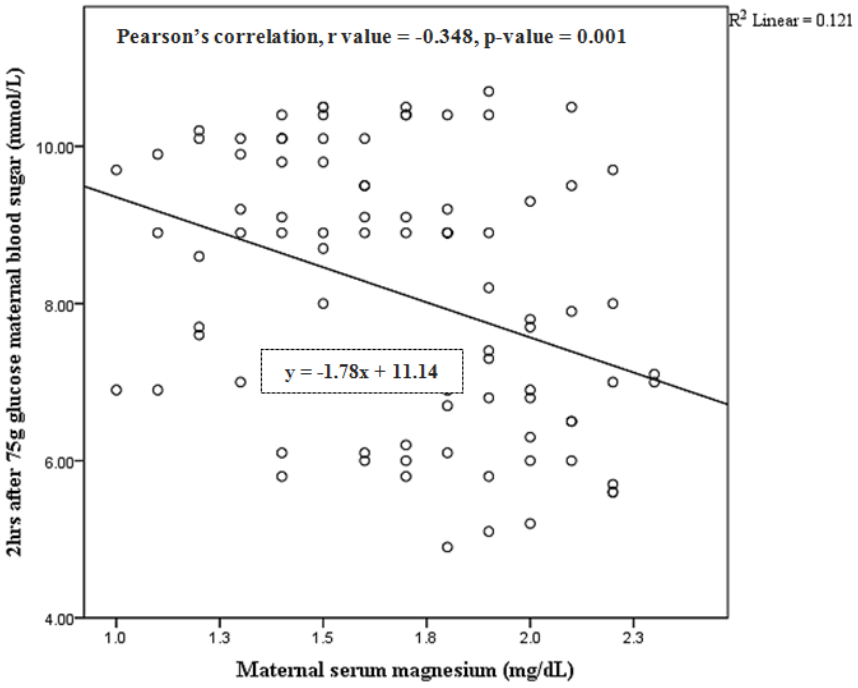

Figure II: Scatterplot diagram showing correlation of the patients according to serum magnesium level with 2hours after 75g of glucose blood sugar (r= -0.348, p=0.001).

R^2 = percentage of variability of 2HA 75g glucose maternal blood sugar due to low serum magnesium level and vice versa
r = Pearson's correlation coefficient

Correlation between maternal serum magnesium level and 2hours after 75g of glucose blood sugar is shown in figure II where significant inverse correlation was observed (r= -0.348, p=0.001).

DISCUSSION

This case-control study was conducted to compare the serum magnesium level in pregnant women with GDM and without GDM as a biochemical marker for risk

estimation and evaluate any association between maternal serum magnesium and GDM. My findings similar to Khan et al. (2013) the monthly income, female occupation, and education level of GDM women were not significantly different from healthy pregnant women.[11] As maternal age was taken match for this study, there mean age distribution was almost similar (case : 26.09 ± 5.05 years and control 25.89 ± 4.85 years. Tamrakar (2014) illustrated that the mean age for GDM was 27.73±4.18 years, and the age-specific prevalence was higher in the 21- 30 group that was about 2.9%.[12]

In this study, most respondents belonged to their third trimester of pregnancy (80.4%). In comparison, primigravida was more in the controls (41.3%), and multigravida patients were included more in the case group (63.0%). Gestational age was taken as matching criteria, with the mean (±SD) gestational age of the respondents was 32.2±5.09 weeks among the cases and 32.0±4.56 weeks in the control group. None of this distribution was statistically significant (p>0.05). In accordance, Huidobro et al. (2010) found that GDM was present in 37.7% of patients in the second trimester and among 38.2% of participants in their third trimester of pregnancy.[13] The women diagnosed late in pregnancy had more family history of type-2 DM. Similar to this study finding, Thathagari et al., (2016) exhibited that nearly 60% of the women with GDM were multigravida, and the remaining 40% were primigravida.[14] Akter et al. (2013) also conducted a cross-sectional study indicating that multiparity or gravidity can risk metabolic syndromes.[15]

At the same time, maternal serum magnesium level was observed significantly low in the cases (1.57±0.28 mg/dL) in comparison to the control group of healthy pregnant participants (1.79±0.33 mg/dL) with the p-value of 0.001. A nearly similar distribution of maternal magnesium levels of 1.55±0.43 mEq/L for GDM cases and 3.01±1.32 mEq/L for pregnant women with normal OGTT were estimated by Vijay (2018).[16]

Odds ratio calculation in the present study revealed, in pregnant mothers, the serum magnesium level < 1.7 mg/dL had 3.22 times more chance to develop GDM compared to that of the pregnant women with magnesium level ≥ 1.7 mg/dL (OR= 3.215; 95% CI=1.368 – 7.557). Therefore, a negative correlation between the GDM women's FBS with maternal magnesium level (r= -0.215, p=0.039) and also 2hrs after 75 g glucose blood sugar level with magnesium (r=-0.348, p=0.001) were observed, denoting that a decline of serum Mg2+ level in pregnant women might result in subsequent rise of blood glucose level. These back our hypothesis that low serum magnesium level is associated with the risk of developing GDM. Several previous study results supported these findings –Rosolová et al. (2000), in their study, found, there was a significant inverse correlation between plasma Mg and steady-state plasma glucose concentrations (r = -0.27, P <.01) in the entire population that indicated lower plasma Mg concentrations associated with increased insulin resistance.[17]

Yang et al. (2014) also investigated serum magnesium levels in women with gestational diabetes. After delivery, subjects were divided into three groups (OGTT with 75 mg unnatural glucose, prediabetes changes, and natural OGTT) and concluded that serum magnesium level in the impaired OGTT group was the lowest among these three groups. However, there was no significant difference in serum magnesium level between mothers with natural OGTT and the group with prediabetes changes.[18]

Ferdous et al. (2019), in their study, estimated the mean serum Mg concentration of GDM patients and in healthy women, where the value was 0.71±0.10 mmol/L and 0.82±0.10 mmol/L, respectively. They also documented that the mean serum concentration of Mg was inversely correlated with mean fasting plasma glucose (8.3 mmol/L) when the 'r' value was -0.577 at p<0.05 level in GDM cases.[19]

A most recent quantitative analytic study by Ambelina et al. (2021) using the cross-sectional comparative design concluded that magnesium level during pregnancy was related to gestational diabetes mellitus incidence, where the mean magnesium level of pregnant mothers with GDM was 1.85±0.12 mg/dL, while in the control sample was 2.10±0.15 mg/dL with p <0.001.[20]

Therefore, in the current study, all the findings showed the association of low magnesium levels among GDM women. So screening for serum magnesium might be considered as a part of the routine antenatal check-up.

CONCLUSIONS

The findings of this study suggest that low maternal serum magnesium level is significantly associated with an elevated risk for the development of GDM.

LIMITATIONS

This study had some limitations as well- The number of study subjects, if higher, would have made the findings more significant.

- The study was conducted in a single hospital. So, the study population might not represent the whole community.
- Sample size was not adequate.
- Therefore, the study findings cannot be generalized to the entire population.

Recommendations

1. Other risk factors of gestational diabetes mellitus should be evaluated.
2. RCT is needed to prove that dietary supplementation of magnesium can prevent gestational diabetes mellitus.

Ethical Issue
The protocol for this study was approved by the institutional review board of insttute of Child & Mother Health.

Conflict of Interest: The Author(s) declared no potential conflicts of interest.

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