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Research Article

Nutritional Aspects of Magnesium in Fetal Growth

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Abstract

Background: Nutrition is the major intrauterine environmental factor that alters expression of the fetal genome and may have future risk of development of diseases in adulthood. Maternal undernutrition during gestation reduces placental and fetal growth of both domestic animals and humans. Maternal Magnesium (Mg) intake is associated with both pregnancy outcome as well as infant outcome.

Methods: The study was conducted in 50 pregnant women aged 17 to 36 years before 20 weeks of gestation and followed till delivery. They were asked to take 1000 mg calcium and 100 mg of elemental iron. Study samples were drawn twice, once before 20 weeks and second within one hour of childbirth. Serum was analyzed for magnesium levels using spectrophotometric method.

Results: Out of 50 pregnant women, only 11 developed preeclampsia on follow up after 20 weeks. In normal pregnant women, mean serum magnesium levels at < 20 weeks of gestation was 2.11 ± 0.31 mg/dL, at term was 2.04 ± 0.31 mg/dl and in cord blood was 1.91 ± 0.29 mg/dl. In preeclamptic women, mean serum calcium levels at < 20 weeks of gestation was 1.80 ± 0.30 mg/dL, at term was 1.61 ± 0.38 mg/dl and in cord blood was 1.61 ± 0.41mg/dl. Correlations between maternal serum magnesium levels and baby weight and Apgar score at 1 minute and 5 minutes in normal pregnancy and preeclampsia were statistically insignificant.

Conclusion: The study data supported the hypothesis that magnesium deficiency might be the causative factor in the development of preeclampsia.

Keywords: Magnesium; Serum; Cord Blood; Outcome; Apgar; Birthweight

Introduction

Many aspects of the mother's health and lifestyle before and during pregnancy have been shown to affect her subsequent pregnancy with potential to impact the health of her child. Maternal nutrition has effects on both fetal growth as well as birth outcomes. Since maternal nutrition is a modifiable risk factor and can be of use in preventing adverse birth outcomes, especially in poor/ low-income women. Maternal nutrition status and dietary intake have significant effects on the outcome of pregnancy in terms of birth weight. Adequate nutritional status before, during and after pregnancy reduces the risk of complications, birth defects and future diseases in off springs during adulthood. A healthy, well-nourished woman is more likely to have a healthy baby having better chances of growing into a healthy child and healthy adult [1].

Since nutrition is a major intrauterine environmental factor influencing the fetal genome expression, this may have lifelong consequences on fetal programming. The theory of "fetal origins of adult disease" states that alterations in fetal nutrition may cause developmental adaptations that predispose the children born to women with the nutritional alterations to future diseases in adult life [2]. Maternal undernutrition during gestation reduces placental and fetal growth of both domestic animals and humans. Available evidence suggests that fetal growth is most vulnerable to maternal dietary deficiencies of nutrients (e.g. protein and micronutrients) during the peri-implantation period and the period of rapid placental development [2].

Nutrition has a major role in both maternal and child health and poor maternal nutritional status has been linked with adverse birth outcomes. Since energy and nutrient demands are increased during pregnancy [3] and body adapts to the increased energy requirements. Micronutrient requirement is increased during pregnancy and their deficiencies can occur due to their losses or malabsorption, inadequate intake or ignorance about prenatal nutrition, or food/dietary taboos practiced during pregnancy have adverse effects on both mothers and newborns [4].

Maternal magnesium intake is associated with both pregnancy outcome and neonatal outcome [5]. Routinely prescribed daily intake of 284.3 mg of magnesium during pregnancy in practice is lower than the recommended allowance [6]. In India, Mg deficiency has been reported in nearly 44% of pregnant women and mothers drinking water containing higher amounts of Mg have been reported to have a reduced risk of low birth weight infants (less than 1,500 g). Magnesium supplementation may be beneficial for the better maternal and fetal outcome. Magnesium supplementation during pregnancy has been associated with fewer maternal hospitalizations, reduced chances of preterm delivery, and neonatal complications. Various clinical trials have reported beneficial effect of oral Mg supplementation during pregnancy reduces the incidence of miscarriage, pregnancy induced hypertension, preterm labor and growth retardation of fetus and magnesium supplementation during pregnancy improved fetal and maternal progress and outcome of pregnancy [5].

Mg deficiency during pregnancy can induce maternal, fetal, and pediatric consequences that might last throughout life. Studies in gestational animals having Mg deficiency has demonstrated its adverse effects on the parturition and post uterine involution. It has been interfered with fetal growth and development and caused morbidity from hematological effects and disturbances in temperature regulation, to teratogenic effects. Premature labor, contributed to by uterine hyperexcitability caused by chronic maternal Mg deficiency that can be intensified by stress, gives rise to preterm birth. If the only cause of uterine over activity is Mg deficiency, its supplementation constitutes nontoxic tocolytic treatment, as an adjuvant treatment, that is devoid of toxicity and enhances efficacy and safety of tocolytic drugs such as beta-2 mimetics. Evidence is considered that Mg deficiency or Mg depletion can contribute to the Sudden Infant Death Syndrome (SIDS) [5].

Serum Mg levels were reportedly lower in women with severe pre-eclampsia than in healthy pregnant women. Magnesium supplementation is used in obstetric practice to prevent the onset of eclampsia and to treat eclampsia. Also, therapeutic administration of Mg affects placental functions namely, vasodilation [7]. Mg sulfate was shown to cause relaxant effect on umbilical arterial tone attenuating the vasoconstrictor effect of angiotensin II and endothelin-1 in the fetal-placental vasculature in an in vitro study of human umbilical artery resistance. Thus, use of magnesium sulfate in treatment of pre-eclampsia or hypertensive disorders of pregnancy has beneficial effects on the fetoplacental circulation. Mg sulfate treatment during pregnancy has a role in calcium homeostasis in preterm newborns [7].

Almonte., *et al*, investigated the effects of magnesium deficiency prior to and during gestation on neonatal morbidity and mortality in rodent model. They observed that magnesium deficiency during pregnancy significantly increases neonatal mortality and morbidity. This was associated with increased incidence of periventricular hemorrhage and edema in newborn pups. Animals before mating were fed a magnesium-deficient diet and after conception they were given magnesium supplementation during pregnancy showed no change in neonatal mortality and morbidity as compared to control animals. The findings of improvement in fetal outcome with dietary magnesium supports the beneficial role of magnesium supplementation during pregnancy [8].

Spätling., *et al.* studied the effect of magnesium supplementation in pregnancy in 568 women who were treated with 15 mmol magnesium-aspartate-hydrochloride per day or aspartic acid as placebo given orally during pregnancy from less than or equal to 16 weeks. Allocation to the two groups was performed according to the women's birthdates. Magnesium supplementation during pregnancy was associated with significantly fewer maternal complications, reduced incidence of preterm delivery, and poor outcome of pregnancy and neonatal complications. The results suggest that magnesium supplementation during pregnancy has reduces fetal and maternal morbidity [9].

Elizabeth., *et al.* explored key anthropometric, biochemical and clinical (ABC) parameters of LBW babies, both preterm and term, compared them with a control group of term normal weight babies. All the measurements namely total protein, albumin, cholesterol, triglycerides, calcium, magnesium, zinc and iron were significantly lower in LBW babies compared to term control babies. Preterm LBW had the lowest values followed by the term LBW. Umbilical cord blood Mg levels were lowest in preterm low birth weight babies, followed by term low birth weight babies and they were highest in term controls. Thus, magnesium levels were lower in low birth weight as compared to normal term control newborns [10].

A cross sectional study was carried out in pregnant subjects with the duration of pregnancy from 28th week of gestation to term of which 42 were normal pregnant women (as control) and 66 were pre-eclamptic (34 with mild and 32 with severe preeclampsia). They observed that serum magnesium levels in normal pregnant group were higher as compared to both mild pre-eclamptic and severe pre-eclamptic groups. It was also observed that serum magnesium of women with mild pre-eclampsia and severe pre-eclampsia were significantly decreased as comparison to control and this decreased serum magnesium level was found to be more in severe preeclamptic compared to mild preeclamptic. These results indicate that reduction in serum levels of magnesium during pregnancy might be a possible contributor in the etiology of preeclampsia and magnesium supplementation in diet or as drugs may be of value to prevent pre-eclampsia [11].

Materials and Methods

The present study was carried out in the Departments of Biochemistry and Obstetrics and Gynecology, Pt. B.D. Sharma, PGIMS, Rohtak in 50 pregnant women (aged 17 to 36 years attending OPD before 20 weeks of gestation) and they were followed till delivery. An informed and written consent was obtained from all these women and the study was approved by Ethical Board of the Institute.

Women with medical disorders and chronic metabolic and endocrinal diseases, epilepsy, severe anemia, were excluded from the study. Calcium and iron supplementation were given to all the pregnant women with period of gestation more than 20 weeks. They were prescribed daily intake of calcium (1000 mg) and elemental iron (100 mg) orally.

Study samples were drawn twice: once before 20 weeks during their visit in OPD and second after delivery within one hour of childbirth. Maternal venous blood (3 ml) was drawn into red vacutainer tubes. Serum magnesium levels were analyzed spectrophotometrically [12].

Statistical analysis

SPSS ver. 23 was used for statistical analysis. Results were expressed as mean ± SD and unpaired't' test and Pearson correlation test was applied.

Results

Only eleven pregnant women developed preeclampsia after the follow up in these women till delivery. Mean age of normal pregnant women was 23.79 ± 2.61 years and pre eclamptic women was 25.63 ±1.91 years. Mean calorie intake of normal pregnant women was 2010.25 ± 161.88 kilocalories/day and pre eclamptic women was 1990.90 ±137.51 kilocalories/day. Mean protein intake for normal pregnant women was 46.97 ± 5.28 gm/day and pre eclamptic women was 45.81 ± 4.77 gm/day.

Mean hemoglobin level was 9.20 ± 0.75 g/dL, mean TSH was 2.17 ± 0.60 mIU/L and mean GCT was 95.46 ± 8.74mg/dL in normal pregnancy. Whereas in pre eclamptic women, mean hemoglobin level was 8.90 ± 2.72 g/dL, mean TSH was 2.05 ± 0.75 mIU/L and mean GCT was 95.54 ± 7.43 mg/dL (Table 1).

Parameters	Normal pregnant women (Mean ± SD)	Pre eclamptic women (Mean ± SD)
Hemoglobin (g/dL)	9.20 ± 0.75	8.90 ± 2.72
TSH (mIU/L)	2.17 ± 0.60	2.05 ± 0.75
GCT (mg/dL)	95.46 ± 8.74	95.54 ± 7.43

Table 1: Hemoglobin, TSH (thyroid stimulating hormone) and GCT (glucose challenge test), (Mean ± SD).

Mean birth weight of baby of normal pregnant women was 2.59 ± 0.48 kg and baby of pre eclamptic women was 2.60 ± 0.51 kg. Mean Apgar score in normal group at 1 min was 6.5 ± 0.49 while at 5 minutes it was 8.7 ± 0.45. Mean Apgar score for pre eclamptic group at 1 min was 6.18 ± 0.6, and at 5 min the score was 8.27 ± 0.64.

Mean serum calcium levels in normal pregnant women (at < 20 weeks of gestation) were 9.37 + 0.78 mg/dL. At term they were 8.95 ± 1.04 mg/dl at term and in the cord blood magnesium levels were 8.54 ± 0.87 mg/dl. In preeclamptic women, mean serum calcium levels (at < 20 weeks of gestation) were 8.16 + 1.19 mg/dL, at term they were 6.40 ± 2.12 mg/dl and in cord blood the levels were 6.03 ± 1.85 mg/dl.

In normal pregnant women (at <20 weeks of gestation), the mean serum magnesium levels were 2.11 + 0.31 mg/dL. They were 2.04 ± 0.31 mg/dl at term levels and in the cord blood the magnesium levels were1.91 ± 0.29 mg/dl. In pre eclamptic women, mean serum calcium levels (at < 20 weeks of gestation) was 1.80 + 0.30 mg/dL, at term it was 1.61 ± 0.38 mg/dl and in cord blood it was 1.61 ± 0.41 mg/dl.

Out of 39 normal pregnant women, 25 had full term normal vaginal delivery, 11 had caesarian section, 2 had assisted vaginal delivery and one had vacuum assisted delivery. Whereas out of 11 pre eclamptic women, 4 had full term normal vaginal delivery, 6 had caesarian section and one had vacuum assisted delivery.

In normal pregnant women, 5 had preterm delivery (i.e., < 37 weeks), whereas in pre eclamptic women, 5 had preterm delivery.

Correlations between maternal serum magnesium levels and baby weight and Apgar score at 1 minute and 5 minutes in normal pregnancy and pre-eclampsia were statistically insignificant (Table 2).

		Serum magnesium at < 20 weeks		**Serum magnesium at term**	
		Correlation coefficient	p value	Correlation coefficient	p value
Baby weight	Normal pregnancy	0.127	0.228	0.052	0.619
	Preeclampsia	0.213	0.527	0.153	0.651
Apgar score at 1 minute	Normal pregnancy	-0.087	0.597	-0.031	0.849
	Preeclampsia	-0.120	0.725	-0.185	0.584
Apgar score at 5 minutes	Normal pregnancy	-0.167	0.306	-0.176	0.283
	Preeclampsia	-0.013	0.967	0.018	0.957

Table 2: Correlations between maternal serum magnesium levels and baby weight and apgar score in normal pregnancy and pre-eclampsia.

Discussion

Magnesium is important in energy requiring metabolic processes, protein synthesis, membrane integrity, nervous tissue conduction, neuromuscular excitability, muscle contraction, hormone secretion and intermediate metabolism. The normal plasma magnesium concentration is 1.5-2.3 mg/dL [13]. Magnesium deficiency may cause uterine hyperexcitability and give rise to preterm birth. Magnesium supplementation constitutes nontoxic tocolytic treatment, which is devoid of toxicity and enhances efficacy and safety of tocolytic drugs such as beta-2 mimetics.

Spätling., *et al*. studied the effect of magnesium supplementation in pregnancy. Magnesium supplementation during pregnancy was associated with significant reduction in preterm delivery [9]. Jafrin., *et al.* in their study reported that the mean serum magnesium of pregnant women with pregnancy induced hypertension was significantly decreased in comparison to that of the control. They noted that mean serum levels of magnesium in normal pregnant group were higher as compared to group with pregnancy induced hypertension, indicating that reduction in serum levels of magnesium during pregnancy might be a possible contributor in the etiology of pregnancy induced hypertension and magnesium supplementation might prevent pregnancy induced hypertension [11].

In the present study, magnesium supplementation was not given to pregnant women. However, the observed changes in serum magnesium values are in agreement with the previous studies.

Elizabeth *et al.* in their study reported that low maternal serum magnesium levels are associated with low birth weight and poor Apgar scores. This discrepancy in results could be attributed to larger sample size in their study (n = 500) [10].

In the present study, there was no significant correlation between maternal serum magnesium levels and birth weight Also the correlation of serum magnesium levels with Apgar score was statistically insignificant (Table 2).

Conclusion

The findings of the present study suggest that magnesium deficiency might be a causative factor in the pathogenesis of pre-eclampsia. The magnesium deficiency might be responsible for the clinical manifestations of these patients in the present study since both magnesium and calcium are important for cellular and neuronal metabolism and cell membrane stability [14].

It can be inferred from the present study that an adequate periconceptional nutrition status is a key determinant of pregnancy outcomes. Dietary modification and geographically relevant nutrition–environment interactions-based intervention might reduce the risk of adverse perinatal outcomes.

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