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The Relationship between Maternal Serum Magnesium Level and Infant Low Birth Weight in Hafez Hospital, Shiraz, Iran

Shahnaz Pourarian[1]*, Bahia Namavar Jahromi[2], Faranak Takmil[3]

[1] Neonatal Research Center, Department of Pediatrics, Nemazee Teaching Hospital, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[2] Department of Obstetrics and Gynecology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[3] Department of Pediatrics, Nemazee Teaching Hospital, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

ABSTRACT

Introduction: There is a great deal of controversy regarding the effect of gestational magnesium (Mg) deficiency on fetal growth and the incidence of low birth weight (LBW) in infants. Therefore, this study aimed to delineate the possible relationship between maternal Mg level and infant LBW.
Methods: This case-control study was conducted on 180 mothers in Shiraz, Iran. Fasting blood samples were obtained for magnesium after delivery. Maternal and neonatal demographic data were recorded, and the mothers were divided into two groups: the control group including mothers with normal-weight infants (≥2500 g), and the case group consisting of mothers with LBW infants (<2500 g).
Results: Out of 90 samples obtained in each group, there was neither a statistical association between the mean maternal magnesium level and neonatal sex (P=0.43) or gestational age (P=0.56), nor a correlation between serum magnesium level and maternal parity (P=0.52), education (P=0.75), or occupation (P=0.59) in the groups. In addition, no significant relationship was observed between maternal serum magnesium level and birth weight in each group (P=0.79).
Conclusion: Due to lack of a statistically significant relationship between magnesium level and birth weight, and considering the contribution of various factors for LBW, more studies are required to investigate the role of other nutrients in infant LBW.

Keywords: Low birth weight, Maternal magnesium, Neonate

Introduction

Magnesium (Mg) is the fourth most common element in the body and the second most essential intracellular cation after potassium. It plays a fundamental role in many physiological reactions such as protein synthesis, while being involved in various metabolic processes such as bone formation (1).

The role of magnesium as an essential element for fetal well-being has been established in obstetrics (2). This element freely crosses the placental barrier and accumulates in the fetus. Therefore, the maternal magnesium content is apparently reflected in the fetus (1).

Due to the increased interest in the role of magnesium in clinical medicine, particularly during pregnancy, many studies have been conducted concerning magnesium deficiency and its consequences during pregnancy. These studies have shown that magnesium deficiency is frequent during pregnancy due to its inadequate or low intake (3). In fact, approximately 44% of pregnant women presented with magnesium deficiency (4).

Studies conducted on animals have revealed that gestational magnesium deficiency has unfavorable effects on both intrauterine fetal growth and hematological system; it also causes disturbance in temperature regulation while having teratogenic results (5-7). Other studies have demonstrated the adverse effects of magnesium deprivation on placental vascular flow. Since magnesium deficiency may reduce placental vascular flow, it is possibly responsible for placental insufficiency, and therefore, it affects the fetal development (8); consequently, it might have a relationship with birth weight.

Considering the aforementioned effects,

* *Corresponding author*: Shahnaz Pourarian, Neonatal Research Center, Department of Pediatrics, Nemazee Teaching Hospital, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran. Tel: 0711-6474298; Mobile: 0917-111-0274; Fax: 0711-6474298; E-mail: porarish@sums.ac.ir

magnesium supplementation during pregnancy is recommended by some studies (9, 10). However, others have shown no correlation between fetal growth retardation, birth weight, and maternal magnesium deficiency during pregnancy (11, 12). Hence, there are yet discrepancies about the relationship between gestational magnesium deficiency and the negative effects on the fetus. Moreover, there is not sufficient reliable evidence to support the efficiency of dietary magnesium supplementation during pregnancy.

The incidence of LBW (<2500 g) has greatly increased in the last two decades, in a way that in year 2010, its prevalence percentage was reported 8.15% in the United States of America (13) and about 8% in Iran (14). Also, regarding the myriads of problems with which these infants are faced, including morbidity and even mortality, finding a way to detect the causes of LBW and decrease its incidence would be of considerable importance for improving maternal and neonatal health and developing neonatal and prenatal care.

Considering the mentioned points and the controversy regarding the effects of gestational magnesium deficiency on fetal growth, we decided to delineate the possible relationship between maternal serum magnesium level and LBW. It would be of great significance to indicate such a relationship and suggest Mg supplements during pregnancy to improve maternal and neonatal health.

Materials and Methods

Patient sample

This case-control study was conducted on mothers delivering in Hafez Hospital (affiliated to Shiraz University of Medical Sciences) in year 2010. The sample was divided into two groups according to the neonatal birth weight. Mothers with LBW infants (<2500g) were selected as the case group, and those with normal-birth-weight newborns (≥2500g) were grouped as the controls.

The medical history of each mother including maternal age, education, occupation, parity, smoking habit, medication use, drug abuse, and significant illnesses was collected. In addition, the newborns' demographic data such as sex, gestational age, birth weight, congenital malformations, and significant recorded illnesses were gathered; such information was recorded in data collection forms.

The gestational age was determined from the mother's chart, based on the ultrasound of the first trimester, and the neonatal birth weight was measured using a digital scale (Tefal Company, France, capacity: 20kg, least count: 10 g, with LED display).

The exclusion criteria were as follows: 1) major systemic disorders or chronic diseases, 2) smoking or drug abuse, and 3) magnesium sulphate intake during pregnancy. Infants with congenital malformations or severe systemic diseases at birth were also excluded. Complications during pregnancy, determined by the medical histories and available medical records, were minimal for all cases. The ethical clearance of the institutional ethics committee as well as the informed consents (from all the participating mothers) were obtained.

Collection of blood samples

Fasting blood samples for magnesium (2cc) were obtained from an antecubital vein using venipuncture procedures within 5 minutes of delivery; they were collected into heparinized tubes and centrifuged for 10 minutes. The centrifugation process and magnesium measurement were conducted in *the* laboratory of Gastroenterohepatology Research Center, affiliated to Shiraz University of Medical Sciences. The serum separated by centrifugation was stored at -80^{o}C until analysis.

Plasma analysis

The analysis of magnesium measurements was performed by a specific colorimetric assay, based on xylidyl blue method (15). By using this method, the normal range of serum magnesium level was measured 1.9 to 2.5 mg/dL in women. Although this procedure is not considered the best colorimetric method (16), it is the most cost effective and available method used in the laboratory of Shiraz Gastroenterohepatology Research Center for magnesium assessment.

Statistical analysis

The collected data were analyzed using SPSS version 16. The mean serum magnesium level of case and control mothers (with neonates of different sexes) were compared by t-test. To detect the relationship between education and mean serum magnesium level in both groups, one-way analysis of variance (ANOVA) was used. Mann-Whitney U test was utilized to determine the relationship between mother's occupation and mean serum magnesium level in both groups. Pearson's correlation coefficient table was finally used to define the correlation between the maternal serum magnesium, gestational age, and neonatal birth weight. *P*-value less than 0.05 was

Table 1. Frequency distribution of demographic characteristics in case and control groups

Variables	Groups		
	Case	Control	*P*-value
***Neonatal* sex (%):**			
Male	37 (45)	34 (42)	
Female	45 (55)	47 (58)	0.43
Gestational age (%):			
≤ 37 wks.	6 (8)	7 (9)	0.5
≥37 wks.	76 (92)	74 (91)	
Maternal demographics			
Age (X±SD)	26.8±4.3	26.16±5.3	0.3
Employment (%):			
Housekeeper	74(90)	75 (92)	0.59
Employed	8 (10)	6 (8)	
Educational level (%):			
E_1*E_2*	23 (28)	35 (43)	
E_3*	45 (55)	33 (41)	
E_4*	14 (17)	13 (16)	0.75
Total	**82**	**81**	

*** E1: uneducated, E2: elementary education, E3: high school and diploma, E4: university graduate**

considered statistically significant.

Results

Out of 90 collected samples in each group, 81 and 82 samples of the control and case groups were used, respectively. Approximately, there was a 10% reduction in the number of samples due to blood hemolysis, which was not measurable; however, this reduction was not statistically significant.

The patient samples were also divided into two groups according to neonatal birth weight. Group A (82 cases) consisted of the mothers of LBW infants with the neonatal birth weight of less than 2500g and the mean weight of 1946±415g. Group B (81 controls) included mothers of normal-birth-weight infants with the neonatal birth weight of more than 2500g and the mean weight of 3157±414g.

Pearson's correlation coefficient between the mean gestational age and the mean maternal magnesium concentration was also calculated. The correlation between the maternal magnesium and the mean gestational age (r=+0.044) in the LBW and control groups (r=+0.048) was not statistically significant (*P*=0.56) (Table 1). Also, the mean magnesium level was compared in infants of both genders in each group using t-test; there were no significant gender-related differences (*P*=0.43) (Table 1).

Mann-Whitney U test indicated no statistically significant differences in the mean serum magnesium level between the housekeepers and working mothers in each group (*P*=0.59) (Table 1). The comparison between the two groups (A and B) showed that the majority of the mothers, who had used the health care facilities in Hafez Hospital, were unemployed. Approximately, 92% and 90% of the subjects in group B and group A were non-workers, hence, both groups were mostly similar in terms of maternal occupation.

The mean serum magnesium level was compared between four maternal education sub-groups (E_1: uneducated, E_2: elementary level education, E_3: high school graduate and diploma, and E_4: university graduate) in both A and B groups; the ANOVA test was utilized for this comparison. The number of mothers in E_1 sub-group was very low, therefore, E_1 and E_2 were considered as one single sub-group ($E_{1,2}$). The majority of the mothers in both groups (A and B) had high school education and diploma, without any university degrees. The mean serum magnesium level was not statistically different between the three sub-groups (*P*=0.75) (Table 1).

The relationship between the mean maternal magnesium level and maternal age was evaluated in each group, using the Pearson's correlation coefficient, and no association was observed (*P*=0.32) (Table 1).

The analysis of variance regarding the effect of maternal parity on magnesium concentration was performed by dividing the mothers in three sub-groups: group 1 with zero previous child delivery, group 2 with one previous delivery, and group 3 with two or more previous deliveries. There was no significant relationship between maternal parity and maternal serum magnesium concentration (*P*=0.52); the case and control groups were mostly analogous in terms of parity. The control and case subjects were mostly matched in terms of neonatal sex, maternal age, education, occupation, and parity. Therefore, there were no significant differences between control and case groups.

The overall mean magnesium level was lower

Table 2. Frequency distribution of the samples in the case and control groups, according to serum magnesium level

Groups	Frequency	Magnesium (mg/dl) (±SD)	*P*-value
Group A (case subjects) (Birth weight < 2500g)	82	2.17 (±0.7)	0.79
Group B (controls) (Birth weight > 2500g)	81	1.98 (±0.6)	

in LBW infants compared to the normal-birth-weight group; however, there was not a statistically significant difference between these two groups (*P*=0.33) (Table 2). The mean magnesium level in both groups was higher than 1.9, and most of them were within the normal range.

Discussion

Neonatal birth weight is a good marker for maternal health and nutritional status. It also plays a key role in indicating the neonatal survival, growth, long-term health, and future psychosocial developments (16). According to Barker's hypothesis, weight at birth is associated with adult metabolic diseases. It might also accelerate the risk of chronic diseases in adulthood, or might be related to hypertension, cardiovascular diseases, or even future glucose intolerance (17). The "fetal origins" hypothesis declares that maternal malnutrition programs the fetus and leads to the reduction of birth weight and later adult-onset diseases (18).

Since preterm and term LBW infants are born with lower nutrient storage at birth, compared to term neonates, supplementation during pregnancy may be required to reach the optimal growth and facilitate better nutrient transfer to the offspring (16); one of these important nutrients is magnesium. On this matter, many recent epidemiological investigations have shown the necessity of magnesium for fetal well-being (4).

It has been shown that gestational magnesium deficiency has several maternal, fetal, and neonatal effects (4), which may remain throughout the neonates' lifetime (18).

A proposed hypothesis suggests that magnesium has an immediate effect on placental vascular flow, and its depletion can have an adverse effect on the placental vascular dilation, which leads to placental insufficiency and is responsible for fetal growth retardation (8). Based on this data, Watson investigated the effect of gestational magnesium intake on newborns, and found a positive correlation between magnesium intake during pregnancy and neonatal birth weight. His study showed that gestational magnesium supplementation could lead to a reduced incidence of LBW (9).

Contrarily, other prospective observational studies, by investigating the relationship between magnesium supplementation and pregnancy outcomes, found no differences between the magnesium-treated group and the placebo. Therefore, according to these studies, magnesium supplementation could not reduce the frequency of fetal growth retardation and preterm labor (12, 19).

In the present study, there was no difference between maternal magnesium level in women with LBW (case) and normal (control) infants (P=0.337). Also, the serum magnesium level in all the mothers was within the normal range, and no differences were observed.

According to one conducted study, when the magnesium intake was restricted to a steady state, the excretion would fall to less than <0.5%, and its tubular reabsorption would increase to compensate the depletion and prevent any alternation in plasma magnesium level (20); this is in agreement with our study results.

A literature review by Azoulay showed that drinking water is one of the significant magnesium sources, which could provide 2 to more than 48 mg per day, depending on water hardness; thus, hard water could be a cardinal source for magnesium intake (21). According to geographical location, water hardness varies from very soft to very hard, and its hardness is deliberated with the level of total calcium; however, magnesium substantially contributes to water hardness (22).

As to the study by Basiri et al. in Shiraz, Iran, water hardness is higher than the normal range (468 ppm), which can be related to high magnesium content (58.6 mg/lit) in drinking water (23). Also, there is evidence that magnesium level is higher in Asian women (24), compared to European (25) and South American women (26). Therefore, the normal range of the mean magnesium concentration in both groups (A and B) of our study might be related to the geographical location and high hardness level of drinking water.

No correlation was found between the mean magnesium level and maternal education (P=0.75) or occupation (P=0.67). The majority of the mothers in our study were not working and had

low educational level, which could be a reflection of their socio-economic status. It seemed that most mothers, who had child delivery in Hafez Hospital, did not belong to the upper socioeconomic class. Accordingly, socioeconomic status might have no association with magnesium concentration in the current study; other studies have revealed similar results (15, 27).
Very limited data is at hand regarding the possible relationship between gestational age and maternal magnesium level. According to Perveen et al., a strong correlation exists between metal concentrations in the cord blood and maternal serum, regarding gestational age (28). The results of our study do not reveal a significant association between maternal magnesium concentration and newborn's sex differences or gestational age.

Conclusion

There were no statistically significant differences between the low and normal birth weight infants in terms of maternal magnesium concentration. However, as many other factors could additively contribute to LBW, more studies are required to investigate other nutrients which could contribute to the incidence of LBW.

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Declaration of interest

The authors declare no conflict of interest.

References

1. Rigo J, Curtis M. Disorder of calcium, phosphate, and magnesium metabolism. In: Martin RJ, Fanaroff A, Walsh MC. Neonatal perinatal medicine. Philadelphia: Mosby; 2011. Pp. 1523-31.
2. Coutts A. Nutrition and the life cycle. 1: Maternal nutrition and pregnancy. Br J Nurs. 2000; 9(17): 1133-8.
3. Baloch GH, Shaikh KH, Jaffary MH. Serum magnesium level during pregnancy. World Appl Sci J. 2012; 17(8):1005-8.
4. Pathak P, Kapoor SK, Kapil U, Dwivedi SN. Serum magnesium level among pregnant woman in rural community of Haryana state, India. European J of Clinic Nutr. 2003; 51:1504-6.
5. Hovdenak N, Haram K. Influence of mineral and vitamin supplements on pregnancy outcome. Eur J Obstet Gynecol Reprod Biol. 2012; 164(2):127-32.
6. Nemato T, Matsuzaki H, Uehara M, Suzuki K. Magnesium-deficient diet-induced in protein utilization in rats is reversed by dietary magnesium supplementation. Mag Res. 2006; 19(1):19-27.
7. Durlach J. New data on the importance of gestational Mg deficiency. J of Am Nutrition. 2004; 23(6):694-700.
8. Takaya J, Yamato F, Kaneko K. Possible relationship between low birth weight and magnesium status: from the stand point of "fetal origin" hypothesis. Magnes Res. 2006; 19 (1):63-9.
9. Watson PE, McDonald BW. The association of maternal diet and dietary supplement intake in pregnant New Zealand women with infant birth weight. Eur J Clin Nutr. 2010; 64(2):184-93.
10. Merialdi M, Carroli G, Villar J, Abalos E, Gülmezoglu AM, Kulier R, et al. Nutritional interventions during pregnancy for the prevention or treatment of impaired fetal growth: An overview of randomized controlled trials. J Nutr. 2003; 133(5 Suppl 2): 1626S-31S.
11. Pathak P, Kapil U. Role of trace elements zinc, copper and magnesium during pregnancy and its outcome. Indian J Pediatr. 2004; 71(11):1003-5.
12. Denguezli W, Faleh R, Hajjaji A, Saidani Z, Letaief M, Haddad A, et al. Maternal nutrition as a determinant of fetal weight: role of trace elements and vitamins. J Gynecol Obstet Bio Reprod. 2007; 38(5): 473-8.
13. Martin JA, Hamilton BE, Ventura SJ, Osterman MJK, Wilson EC, Mathews TJ. Births: final data for 2010. Natl Vital Stat Rep. 2012; 61(1):1-65.
14. Naghavi M. Transition in health status in Islamic Republic of Iran. Iran J Epidemiol. 2006; 3:13-25.
15. Varley H, Gowenlock AH, Bell M, eds. Practical clinical biochemistry. 6th ed. UK: Amazon Co; 2002. p. 361-462.
16. Elizabeth KE, Krishnan V, Vijaykumar T. Umbilical cord blood nutrients in low birth weight babies in relation to birth weight and gestational age. Indian J Med Res.2008; 128:128-33.
17. Robinson SM, Barker DJP. Coronary heart disease: a disorder of growth. Proc Nutr Soc. 2002; 61(4): 537-42.
18. Takaya J, Kaneko K. Small for gestational age and magnesium in cord blood platelets: Intrauterine Magnesium deficiency may induce metabolic syndrome in later life. J Pregnancy. 2011; 2011: 270474.
19. Makrides M, Crowther CA. Magnesium supplementation in pregnancy. Cochrane Database Syst Rev. 2001; 4(4):CD000937.
20. Swaminathan R. Magnesium metabolism and its disorders. Clin Biochem Rev. 2003; 24:47-66.
21. Azoulay A, Garzon PH, Eisenberg MJ. Comparison of the Mineral content of tap water and bottled waters. J Gen Intern Med. 2001; 16(3):168-175.
22. Yang CY, Chiu HF, Tsai SS, Chang CC, Sung FC. Magnesium in drinking water and the risk of delivering a child of very low birth weight. Magnes Res. 2002; 15(3-4):207-13.

23. Basiri A, Shakhssalim N, Khoshdel AR, Pakmanesh H, Radfar MH. Drinking water composition and incidence of urinary calculus. Iran J kidney Dis. 2011; 5(1):15-20.
24. Baig S, Hasnain NU, Ud-din Q. Studies on Zn, Cu, Mg, Ca and Phosphorus in maternal and cord blood. J Pak Med Assoc. 2003; 53(9):417-22.
25. Molina-Montes E, Sánchez-Cantalejo E, Martínez C, Contreras JM, Molina E, Sánchez MJ. Compliance with dietary and nutrient recommendations in the European Prospective Investigation into Cancer and Nutrition (EPIC)- Granada Cohort at recruitment. Nutr Hosp. 2012; 27(2):572-82.
26. De la Cruz-Góngora V, Gaona B, Villalpando S, Shamah-Levy T, Robledo R. Anemia and iron, zinc, copper and magnesium deficiency in Mexican adolescents: National Health and Nutrition survey 2006. Salud Publica Mex. 2012; 54(2):135-145.
27. Kozielec T, Durska G, Karakiewicz B. Analysis of blood and hair to investigate the magnesium status of neonates and their mothers. Magnes Res. 2004; 17(2): 85-9.
28. Perveen S, Altaf W, Vohra N, Bautista ML, Harper RG, Wapnir RA. Effect of gestational age on cord blood plasma, copper, zinc, magnesium and albumin. Early Hum Dev. 2002; 69:15-23.