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The Association Between Low Maternal Serum Magnesium Levels and Preterm Labor

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Abstract

Background and objective: Preterm labor is the main cause of neonatal mortality and morbidity, which can be attributed to various factors. The specific effects of magnesium sulfate in preterm labor include its function as a tocolytic agent, suppressing uterine contractions to delay delivery and allow time for administering corticosteroids, which aid in fetal lung maturation. This study aimed to determine the association between premature labor and blood magnesium levels.

Methods: The present study was a case-control study conducted at the Sulaymaniyah Maternity Teaching Hospital in Sulaymaniyah City, Kurdistan Region, Iraq, over a period of one year, from May 1, 2022, to April 31, 2023. One hundred pregnant women who presented to the labor ward with contractions were divided into two study groups: 50 pregnant women delivered before 36+6 weeks (case group) and 50 pregnant women delivered after 37 weeks (control group). Magnesium blood levels were measured in both groups.

Results: Forty percent of patients exhibited varying degrees of hypomagnesaemia. It was observed that 56% of the case group had serum magnesium levels below 1.6 mg/dl, while only 24% of control patients had such low serum magnesium levels. The relative risks indicated that patients with low serum magnesium concentrations (<1.6 mg/dl) had a 2.333 times higher risk of preterm delivery compared to those with normal magnesium levels.

Conclusion: Pregnant women with low serum magnesium levels are at an increased risk of experiencing preterm labor.

Keywords: Magnesium deficiency, Preterm labor, Uterine contraction

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Introduction

A labor that involves frequent and regular uterine contractions and causes progressive changes in the cervix before the full 37 weeks of pregnancy is called preterm labor. In general, preterm births account for 10 to 15 percent of all deliveries.[1] Preterm labor will lead to some long-term complications such as hearing and vision impairment, growth delay, and cerebral palsy in the child, which can subsequently lead to early childhood disabilities.[2]The pathogenesis of preterm labor (about 1/3) is unknown. But factors related to lifestyle, genetic issues, uterine structural disorders, amniotic fluid infection, and a lack of some minerals, including magnesium, may be involved in the occurrence of preterm labor.[3] Magnesium is a divalent cation and cofactor of more than 300 enzymes and the fourth most vital cation in the body, and protein S is required for nerve function, energy metabolism, nucleic acid synthesis, and muscle contraction.[4] Magnesium plays an essential role in various physiological processes, including muscle relaxation and the prevention of preterm contractions. 99% of the body's magnesium is inside the cells and in the skeleton, and as it were, 1% of the body's magnesium is within the extracellular fluid. But only extracellular magnesium can be easily measured which is normally (1.6-2.2) md/dl, and in other words, magnesium (<1.6 mg/dl) indicates a decrease in magnesium in the whole body. According to previous reports, uterine muscle cell hyperactivity was correlated with magnesium deficiency in pregnant women, and this can potentially increase the risk of spontaneous abortion, preeclampsia, and preterm labor.[5, 6]The correlation between preterm labor and serum magnesium levels has been studied in some research studies.[4, 6] Intravenous administration of magnesium sulfate, specifically to women at risk of preterm labor, demonstrates a reduction in the incidence of preterm labor. The specific effects of magnesium sulfate in preterm labor include: Magnesium sulfate functions as a tocolytic agent, meaning it suppresses uterine contractions, aiming to delay delivery and buy time for administering corticosteroids, which help in fetal lung maturation. By relaxing the uterine muscle, it may help postpone labor for a short period of time.[17] Neuroprotection: Magnesium sulfate has been found to have neuroprotective properties for the unborn child, particularly in cases of preterm birth where there is a risk of cerebral palsy. Studies suggest that magnesium sulfate administration to mothers at risk of preterm delivery may reduce the likelihood of cerebral palsy in the newborn.[18] Healthcare providers determine its appropriateness and dosage based on the gestational age, maternal condition, and the risks associated with preterm labor.[19] Some studies have suggested that low levels of blood magnesium during pregnancy may be associated with an increased risk of preterm birth .[4-7] However, the evidence is not consistent, and additional research is needed to confirm this relationship.[5] While magnesium supplementation during pregnancy is often recommended to prevent or treat conditions like preeclampsia, its direct impact on preterm labor is still not fully established.[8] It's important to note that the correlation between blood magnesium levels and preterm delivery can vary among individuals. Other factors, such as overall health, genetics, and lifestyle choices, may also influence the risk of preterm labor. In vitro studies have shown that magnesium inhibits the entry of calcium into the cell by competing with calcium in the motor end plate or on the cell membrane level, and in this way, it can reduce uterine contractions.[9] Unfortunately, during pregnancy, the concentration of total magnesium has a clear decrease compared to non-pregnant women, and therefore, the decrease in serum

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magnesium is due to the physiological cause of pregnancy (such as failure to receive uncooked vegetables, etc.).[10] It should be noted that uncooked vegetables (dark color) are a good source of magnesium.[20] Nuts and legumes are relatively high in magnesium. But the consumption of some foods, such as spinach, can prevent the absorption of magnesium. However, more than 20% of people in the world receive less than the recommended amount of magnesium. Along with other background causes, this increases the basis for the occurrence of hypomagnesaemia in the excitability of the uterine muscle (of course, since pregnancy is accompanied by hypokalemia, it is possible that hypokalemia and hypomagnesaemia are involved in the excitability of the uterus). [10, 17] The aim of the study was to find the relationship between a low serum magnesium level and the onset of preterm labor.

Patients and methods

The present study was a case-control study conducted at the Sulaymaniyah Maternity Teaching Hospital in Sulaymaniyah City, Kurdistan Region, Iraq, for 1 year, from May 1, 2022, to April 31, 2023.The studied population was one hundred pregnant women, which were divided into two study groups (50 pregnant women of gestational age were between 28 and 36 weeks [case group] and 50 pregnant women of gestational age were ± 37 weeks [control group]). The inclusion criteria's taken were women with singleton pregnancies of gestational ages from 28 weeks and more coming with the onset of labor. The exclusion criteria were multiple gestations, IUGR (intrauterine growth restriction), medical diseases, history of preterm labor, rupture of membrane, administration of intravenous or intramuscular magnesium sulfate to prolong labor (because they are all risk factor of preterm labor), and refusal to participate. The Kurdistan Higher Council of Medical Specialties and Hospital Authority's recorded approval, the patients' consent, data confidentiality, and appropriate care of complications all contributed to the implementation of the study ethics. Information about patients was collected by the researcher directly from selected women. The questionnaire contains general characteristics of study participants (age, socioeconomic status, residence, occupation, body mass index, gravidity, parity, miscarriage, and gestational age), women's obstetrical history, medical and surgical history, and magnesium level of study participants. The serum magnesium level was measured by collecting blood samples from study participants, which were sent to the Laboratory of Maternity Teaching Hospital for analysis, and a cutoff value of <1.6 was considered hypomagnesemia. The "IBMIBMSS Statistics version 25" program was used for the analysis of the data. Besides, a p value of ≤0.05 was considered a statistically significant association. Also, descriptive and inferential statistics were used for the analysis of the data. Composed educated consent was obtained from the participants before their enrollment in the study. In addition, the researcher herself obtained consent after an explanation of the detailed procedure to be taken.

Results

The demographic information of the respondents to the questionnaire is given in Table (1). As shown in Table (1), there was no significant difference between both groups in relation to demographic characters except residence (p= 0.025).

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Table (1): Demographic characteristics

Characteristics	Cases N (%)	Control N (%)	p value
Age (year)			
20-29	28 (56.0)	25 (50.0)	0.534
30-35	12 (24.0)	17 (34.0)	
>35	10 (20.0)	8 (16.0)	
Socioeconomic Status			
Low	20 (40.0)	16 (32.0)	0.486
Middle	21 (42.0)	27 (54.0)	
High	9 (18.0)	7 (14.0)	
Residency			
Rural	35 (70.0)	24 (48.0)	0.025
Urban	15 (30.0)	26 (52.0)	
Occupation			
Unemployed	36 (72.0)	29 (58.0)	0.142
Employer	14 (28.0)	21 (42.0)	
Body mass index (kg/m^2)			
<18.5	1 (2.0)	2 (4.0)	0.836
18.5-24.9	21 (42.0)	24 (48.0)	
25-29.9	13 (26.0)	9 (18.0)	
30-34.9	11 (22.0)	12 (24.0)	
≥35	4 (8.0)	3 (6.0)	
Gravida			
Primigravida	17 (34.0)	20 (40.0)	0.534
Multigravida	33 (66.0)	30 (60.0)	
Total	50 (100.0)	50 (100.0)	

Table (2): Association between serum magnesium and preterm labor

Serum magnesium	Cases N (%)	Control N (%)	Total N (%)	p value
<1.6 mg/dL	28 (56.0)	12 (24.0)	40 (40.0)	0.001
≥1.6 mg/dL	22 (44.0)	38 (76.0)	60 (60.0)	
Total	50 (100.0)	50 (100.0)	100 (100.0)	

Relative risk= 2.333 (95% CI-1.345-4.049)

According to the results obtained, 40% of woman suffers from hypomagnesaemia of varying degrees Table (2). They also found that 56% of study participant had serum magnesium levels below 1.6 mg/dl, while only 24% of control participant had serum magnesium levels this low. The RR (relative risk) shows that the risk of preterm delivery was 2.333 times higher in woman with low serum magnesium levels (<1.6 mg/dL). Statistically, the difference in serum magnesium levels between both groups was significant (p value = 0.001).

Table (3): Difference between serum magnesium and gestational age at onset of labor

Gestational age at delivery (weeks)	Serum magnesium levels		p value
	<1.6 mg/dL N (%)	≥1.6 mg/dL N (%)	
28-32+6	7 (25.0)	8 (36.36)	0.543
33-34+6	5 (17.85)	2 (9.09)	
35-36+6	16 (57.14)	12 (54.54)	
Total	28 (100.0)	22 (100.0)	

Evaluation of the gestational age distribution of women with preterm birth showed that there was no significant difference in the normal and reduced serum magnesium levels groups Table (3). Also, obstetrical (e.g., PROM (premature rupture of membrane), PPROM (preterm PROM), UTI (urinary tract infection), PET (pre-eclamptic toxemia), GDM (gestational diabetes mellitus), and IUGR problems, as well as current medical (e.g., diabetes mellitus, hypertension), were not observed in any cases.

Discussion

Magnesium deficiency during pregnancy can have various negative impacts on both the mother and the developing baby. Some important aspects to consider are gestational hypertension, preterm labor, fetal growth restriction, muscle cramps, gestational diabetes, and postpartum depression. It is

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essential for pregnant women to maintain adequate magnesium levels through a balanced diet or supplements (if recommended by their healthcare provider). Food sources of magnesium include green leafy vegetables, whole grains, nuts, seeds, and legumes. In this study, 56% of the people who had preterm labor were in the age range of 20–29 years. Also, 6% of people who had preterm labor had multiple births. 56% of the people under study who had preterm labor had a magnesium serum level less than 1.6 mg/dL. In addition, among the people whose serum level was less than 1.6 mg/dL, 57.14% of them had preterm labor at 35–6 weeks. Similar to the results reported by Rahman *et al*., and Okunade *et al*., the difference between the maternal ages of the cases was not significant. [4 ,11]This study showed that the serum level of magnesium is significantly lower in women with preterm labor than in healthy pregnant mothers (less than 1.6). Kamal and colleagues also obtained similar results during a three-group study in India among healthy pregnant mothers and non-pregnant women.[12] As previous results have shown, magnesium decreases in the course of a normal pregnancy.[2-5] Pathak and his colleagues also showed in their studies that 44% of pregnant women have lower than normal serum magnesium levels.[13] In the present study, 24% of the control group had serum magnesium levels lower than normal. Observations have shown that magnesium deficiency affects the fetus in addition to increasing the probability of preterm labor. Kovac and Tany studies showed that hypomagnesemia in the mother can lead to IUGR and LBW (low birth weight).[14, 15] In their subsequent investigation, they found that a daily intake of 15 mmol of magnesium aspartate during pregnancy can reduce IUGR and LBW.[14] Classen and colleagues also suggested that magnesium supplementation during pregnancy would be beneficial in order to reduce the frequency of miscarriage.[16]

Conclusion

Reduced magnesium levels were associated with preterm birth. Patients with low serum magnesium levels are at risk of having preterm labor, so we recommend that during pregnancy, treating magnesium deficiency may play a factor in reducing preterm labor, at least in those patients who are at risk of preterm labor.

Disclosure:

The authors assert that they have no conflicts of interest.

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