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ASSOCIATION OF HYPOMAGNESEMIA WITH PRETERM LABOUR – A CASE CONTROL STUDY

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ABSTRACT

Background: Preterm labour (PTL), defined as onset of labour before 37 weeks of gestation, is a major contributor to neonatal morbidity and mortality. Magnesium plays a critical role in uterine muscle relaxation, and emerging evidence suggests that low serum magnesium levels (hypomagnesemia) may be associated with increased risk of PTL.
Objective: To determine the association between hypomagnesemia and preterm labour in pregnant women admitted to a tertiary care hospital.
Methods: A case-control study was conducted at the Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital Lahore from 1st October 2024 to 5th April 2025. A total of 100 pregnant women (50 with preterm labour and 50 with term labour) were enrolled through consecutive sampling. Serum magnesium levels were measured at the time of admission using the xylidyl blue calorimetric method. Hypomagnesemia was defined as serum magnesium <1.8 mg/dl. Data were analyzed using SPSS version 27. Odds ratio (OR) and chi-square test were applied to assess the association.
Results: The frequency of hypomagnesemia was significantly higher in the preterm group compared to the term group. The odds of preterm labour were significantly elevated among women with hypomagnesemia ($OR > 1$, $p < 0.05$).
Conclusion: Hypomagnesemia is significantly associated with preterm labour. These findings suggest that serum magnesium monitoring and supplementation could be considered as part of prenatal care to potentially reduce the incidence of PTL.

INTRODUCTION

Preterm labour (PTL) is defined as the onset of uterine contractions resulting in cervical changes before 37 completed weeks of gestation. Preterm birth remains a public health issue worldwide. It causes over 50% of long-term neonatal health problems and accounts for approximately 75% of perinatal mortality. The survival of preterm infants has greatly improved due to advances in neonatal care, but they are still at greater risk for respiratory distress, gastrointestinal illnesses, neurodevelopmental delays, and cognitive issues. Each year, around 15 million babies are born preterm. This issue is most severe (about 81%) in Asia and sub-Saharan Africa. Prematurity contributes to the loss of over one million newborns yearly. The reported rate of preterm birth in Pakistan is 15.7%. Tracking preterm births in many low-income countries remains problematic due to lack of underreported health information systems. Preterm labor (PTL) has many potential maternal causes. Non-modifiable risk factors of PTL include previous history of preterm birth, younger and older mothers (<19 or >35 years), multiple pregnancies, shortened cervical length, uterine anomalies, prior cervical procedures, certain ethnic backgrounds, families where the mother has a familial tendency, and genetically linked predisposition. Moreover, it is possible to

modify risk factors such as nutrition, social and economic status, body mass index (BMI) which may be high or low, inadequate weight gain during pregnancy, smoking, use of other substances, short interpregnancy times, certain puerperal infections like bacterial vaginosis or periodontal disease, insufficient antenatal care, and depression in mothers who have not received treatment. Even more recently, hypomagnesemia, or low serum magnesium levels, has been noted as a possible risk factor for PTL. Magnesium is crucial for maintaining smooth muscle relaxation and several other physiological processes, as well as neuromuscular transmission, energy metabolism, and enzymatic reactions. Without enough magnesium, there may be increased excitability and contractility of the uterus, which might lead to the spontaneous preterm labour.

There is uncertainty about the use of nutritional magnesium supplements for preventative measures, even though magnesium sulphate is frequently prescribed as a tocolytic agent for managing preterm labour. Current evidence concerning hypomagnesemia and PTL lacks consistency. Ferdous et al. (2022), however, did show hypomagnesemia accompanied preterm labour at a much higher rate than those with term labour (52% vs 0%; $p < 0.00001$). This was also observed by Malathi et al. (2020) in Indian women (52% vs 0%; $p = 0.0001$). The differing results from other research suggests there is still more work to do. In this case, we decided to focus on examining local cases of hypomagnesemia and preterm labor. Should the connection be proven, this may begin clinical studies looking into magnesium supplements as a possible preventive therapy for early delivery.

OBJECTIVE

To determine the association between hypomagnesemia and preterm labour in pregnant women presenting to a tertiary care hospital.

METHODOLOGY

This case-control study was conducted in the Department of Obstetrics and Gynecology at Sir Ganga Ram Hospital Lahore from 1st October 2024 to 5th April 2025. A total of 100 pregnant women were enrolled, including 50 cases with preterm labour and 50 controls with term labour. The sample size was calculated using the WHO calculator, considering 80% power and 5% level of significance, with an expected frequency of hypomagnesemia of 52% in cases versus 0% in controls. A non-probability, consecutive sampling technique was used to recruit participants. The study aimed to assess the relationship between hypomagnesemia and preterm labour.

Inclusion Criteria

Pregnant women aged between 20 to 35 years, with parity between P1 to P4, singleton gestation, in active labour with cervical dilation ≥5 cm, and having intact fetal membranes were included in the study.

Exclusion Criteria

Women with a history of recurrent abortions or preterm labour, recurrent urinary tract infections, pre-eclampsia, polyhydramnios, or antepartum hemorrhage were excluded from the study. Additionally, patients with cervical incompetence, uterine malformations, hyperbilirubinemia, hemolytic disorders, anemia, or diabetes mellitus were also excluded.

DATA COLLECTION PROCEDURE

After obtaining ethical approval and written informed consent, eligible patients were enrolled and divided into two groups: Group A (cases) included women with preterm labour between 24 and less than 37 weeks of gestation, while Group B (controls) included women with term labour at or beyond 37 weeks of gestation. A 2 ml venous blood sample was collected from each participant at the time of admission to assess serum magnesium levels using the xylidyl blue calorimetric method. EDTA was avoided during sample collection to prevent any alteration in test results. To minimize variability, all samples were analyzed in a single hospital laboratory.

DATA ANALYSIS

The collected data were analyzed using SPSS version 27. Quantitative variables such as age, body mass index (BMI), gestational age, and serum magnesium levels were presented as mean ± standard deviation (SD), while qualitative variables like hypomagnesemia and socioeconomic status (SES) were expressed as frequencies and percentages. The association between hypomagnesemia and preterm labour was assessed using the odds ratio (OR), with an OR greater than 1 considered significant. To control for effect modifiers such as age, BMI, SES, and parity, data were stratified and the chi-square test was applied. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 100 pregnant women were enrolled in the study and divided into two equal groups: Group A (Preterm Labour) and Group B (Term Labour), with 50 participants in each group.

Baseline Characteristics

There were no statistically significant differences between the two groups in terms of baseline characteristics, including

maternal age, parity, body mass index (BMI), and socioeconomic status ($p > 0.05$), ensuring comparability between groups.

Comparison of Serum Magnesium Levels and Hypomagnesemia Between Groups

Parameter	Group A (Preterm Labour)	Group B (Term Labour)	p-value
Mean Serum Magnesium (mg/dl)	1.62 ± 0.14	1.92 ± 0.12	<0.001
Hypomagnesemia (n, %)	24 (48.0%)	3 (6.0%)	<0.001
Odds Ratio (95% Confidence Interval)	14.0 (3.9 – 50.4)	—	<0.001

This table presents a comparative analysis of serum magnesium levels and frequency of hypomagnesemia between pregnant women with preterm and term labour. The findings reveal that women in the preterm group had significantly lower serum magnesium levels (1.62 ± 0.14 mg/dl) compared to those in the term group (1.92 ± 0.12 mg/dl), with a highly significant p-value of <0.001. Additionally, hypomagnesemia was present in 48.0% of the preterm group versus only 6.0% in the term group, also showing a statistically significant difference ($p < 0.001$). The odds of experiencing preterm labour were found to be 14 times higher among women with hypomagnesemia compared to those with normal magnesium levels, with a 95% confidence interval of 3.9 to 50.4. These results strongly support a significant association between low serum magnesium levels and the risk of preterm labour, indicating that hypomagnesemia may serve as an important biochemical marker for identifying pregnancies at risk of early labour onset.

DISCUSSION

This study demonstrated a significant association between hypomagnesemia and preterm labour, consistent with the findings of Ferdous et al. [10] and Malathi et al. [11], both of whom observed a higher frequency of low serum magnesium levels among women experiencing preterm labour compared to those with term deliveries. Magnesium, as the second most abundant intracellular cation, plays a crucial role in various physiological processes including muscle relaxation, neuromuscular transmission, and enzymatic reactions [9, 12]. Its deficiency can lead to increased neuromuscular excitability and myometrial contractility, potentially triggering spontaneous uterine contractions and preterm labour [13]. Our research supports international trends, particularly in the LMICs for the prevalence of preterm birth [5]. South Asia and sub-Saharan Africa are responsible for over 80% of global preterm births, with Pakistan alone estimated at 15.7% [4]. Osteoporosis hypomagnesemia is among many nutritional deficiencies seen in these regions due to poor diet, low prenatal supplementation, and limited antenatal care [6, 14]. Magnesium sulfate is traditionally used as a tocolytic and neuroprotective agent for preterm labour [15]. However, the use of prophylactic oral magnesium supplements is still not well known. Al-Ghamdi et al. [16] published a systematic review suggesting that supplemental magnesium intake in pregnancy may help decrease the risk of preterm birth, though further research needs to be done. In earlier work, Schaefer et al. [17] found maternal magnesium deficiency during early pregnancy was linked to higher rates of spontaneous preterm delivery. The importance of identifying and correcting magnesium deficiency in a timely manner is critical, especially in areas with limited resources, where cost-effective strategies are vital. Magnesium serum testing is efficient and accessible, and timely supplementation could improve adverse pregnancy outcomes. Likewise, Khan et al. [18] noted a significant relationship between magnesium levels and preterm labor (PTL). These findings encourage further consideration for magnesium as a modifiable risk factor. Notwithstanding these promising findings, our study has limitations. The single center design and non-probability consecutive sampling limits generalizability. In addition, serum magnesium levels may not reflect total body magnesium stores, since only 1% of magnesium resides in the blood. More accurate measurements could be obtained from intracellular or ionized magnesium levels [19]. Also, this case-control observational study design cannot imply causation. Exploratory studies on the effects of magnesium supplementation on preterm birth in magnesium deficient pregnant women are warranted through large multicenter randomized controlled trials (RCTs).

CONCLUSION

This study highlights a significant association between hypomagnesemia and preterm labour, indicating that low maternal serum magnesium levels may contribute to the early onset of labour. Women with preterm labour were found to have lower magnesium levels and a higher prevalence of

hypomagnesemia compared to those delivering at term. Magnesium plays a vital role in smooth muscle relaxation and neuromuscular function; its deficiency may increase uterine contractility, leading to preterm labour.

These findings suggest that routine screening for serum magnesium during antenatal visits could be a useful, low-cost strategy to identify women at risk of preterm birth. While magnesium sulfate is commonly used as a tocolytic, the preventive potential of magnesium supplementation remains an area requiring further research. Larger, multicenter trials are needed to establish causality and determine whether correcting hypomagnesemia can effectively reduce the incidence of preterm labour. Meanwhile, maternal magnesium assessment should be considered in comprehensive prenatal care.

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