

A COMPARATIVE STUDY OF SERUM MAGNESIUM LEVEL IN PRETERM LABOR AND TERM LABOR

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Abstract

Background: Preterm birth is a major cause of perinatal mortality and morbidity, accounting for 70–80% of perinatal deaths in India. Hypomagnesemia, which is associated with uterine hyperactivity and cervical dilatation, increases the risk of infection. This study aimed to determine the association between serum magnesium levels and preterm delivery. **Materials and Methods:** This cross-sectional study included 160 women, conducted at the Government Stanley Medical College from March to November 2021. Group A (n=80) included preterm labor (28–36 weeks) and Group B (n=80) included term labor (≥ 37 weeks). Serum magnesium levels were measured using the colourimetric xylidyl blue method with the COBAS C system. Venous blood (2 ml) was collected upon admission to avoid EDTA interference, with the normal magnesium range set at 1.6–2.6 mg/dl. **Result:** The mean serum magnesium levels were significantly lower in preterm pregnancies (<34 weeks: 1.031 ± 0.311 mg/dl, >34 weeks: 1.293 ± 0.346 mg/dl) than in term pregnancies (<39 weeks: 1.07 ± 0.369 mg/dl, >39 weeks: 1.731 ± 0.243 mg/dl, $p < 0.001$). For cervical dilation <3 cm, preterm levels (1.134 ± 0.332 mg/dl) were lower than term levels (1.587 ± 0.377 mg/dl, $p < 0.001$). Neonatal complications, such as respiratory distress (35% vs. 1.3%), jaundice (52.5% vs. 3.8%), and mortality (6.3% vs. 0%) were significantly higher in preterm births than in term births ($p < 0.001$). Meconium and IUGR rates were also elevated in preterm neonates; 6.3% in the preterm group died, while no neonatal deaths were observed in the term group. **Conclusion:** Hypomagnesemia was significantly associated with preterm labor independent of age or parity. Serum magnesium estimation is a cost-effective predictor, and supplementation may help prevent preterm labor and its complications.

INTRODUCTION

Preterm birth is defined as birth between the age of viability, i.e., between 28 weeks and 37 completed weeks of gestation. Preterm births have been given more attention as they are the major leading cause of perinatal and neonatal mortality and morbidity, comprising 50%, and there are many short- and long-term complications associated with low birth weight due to preterm birth. Although all births before 37 weeks of gestation are considered premature, births before 32 weeks of gestation account for most neonatal deaths and disorders.^[1]

The incidence of preterm labor in India is 5-10%, leading to 70%-80% perinatal deaths. The use of modern technology allows the survival of many preterm neonates in developed countries; however, such care is not widely available in developing countries. Late preterm births account for about 74% of all preterm births, while early preterm births are

2% of all births and remained constant during the last two decades.^[2,3]

The causes of preterm labor are not completely known; in 50% of the cases, it is spontaneous and idiopathic, although several potential risk factors have been identified. The main cause is Premature Rupture of Membranes (PROM), which is up to 30%, and another 15-20% is secondary to conditions such as multiple pregnancies, polyhydramnios, infection, uterine anomalies, cervical incompetence, antepartum haemorrhage, hypertensive disorder of pregnancy, anaemia, smoking, fetal abnormalities, and IUD. It is also related to socioeconomic status & geographic location.^[4-6]

Besides these aetiologies, preterm labor is also due to a biochemical alteration of body function at the cellular level of trace elements such as magnesium, the second most abundant intracellular cation after potassium.^[7,8] It plays several vital physiological and biochemical roles; intracellular ionized magnesium is essential for nerve conduction and muscle contraction.^[9] The inhibitory effect of magnesium on

preterm labor causes antagonism of calcium-mediated uterine contractions; magnesium acts on uterine myometrium, causing it to relax by stimulating alpha-2 adrenergic receptor and cyclic AMP and hence, it is used as a tocolytic.^[10]

Hypomagnesemia causes neuromuscular hyperexcitability, leading to muscle cramps and uterine hyperactivity. This leads to increased cervical dilatation, which in turn facilitates the approach of vaginal microorganisms and changes the quality and quantity of vaginal discharge colonized by pathogenic microorganisms. Predicting and preventing preterm labor should be emphasized to prevent morbidity and mortality due to preterm births. Hence, this study evaluated the relationship between serum magnesium and preterm labor so that morbidity and mortality due to prematurity could be reduced by early diagnosis of its deficiency and its correction.

Aim: This study aimed to correlate serum magnesium levels between preterm and term deliveries.

MATERIALS AND METHODS

This analytical cross-sectional study, which included 160 women, was conducted in the Department of Obstetrics and Gynaecology, Government Stanley Medical College and Hospital, for eight months from March 2021 to November 2021. The Institutional Ethics Committee approved the study before initiation, and informed consent was obtained from all patients.

Inclusion criteria

For Group A, women aged 18–35 years with singleton pregnancies, gestational age between 28 and 36 weeks, painful uterine contractions (more than two within 30 minutes), and cervical dilatation (at least 2 cm) with effacement were included.

For Group B, pregnant women aged 18–35 years with singleton pregnancies after completing 37 weeks of gestation who experienced labor pain were included.

Exclusion criteria

In Group A, women with known factors associated with premature labor, such as pregnancy with fibroid uterus, hypoplastic uterus, or other uterine abnormalities, prior tocolysis, multiple pregnancies, ruptured membranes, placenta previa, incompetent cervix, known or detected fetal anomalies, and polyhydramnios were excluded.

In Group B, women with major diseases such as diabetes or preeclampsia/eclampsia, a history of prior tocolytic agent use, or conditions such as placenta previa were excluded.

Methods

The patients were selected using a consecutive sampling method and divided into two groups: Group A (cases; n=80) with preterm labor between 28 weeks and 36 gestational weeks and Group B (control; n=80) with term labor after 37 completed gestational weeks.

Serum magnesium levels were measured using the colourimetric endpoint method, an in vitro test for quantitatively determining magnesium in human serum using Roche/Hitachi COBAS C systems. This test involves magnesium forming a purple complex with xylydyl blue and diazonium salts in an alkaline solution. The Mg concentration was determined photometrically by measuring the decrease in the absorbance of xylydyl blue.

For sample collection, 2 ml of venous blood was drawn from both patients and controls upon admission to the labor ward. The collected serum was analysed in the laboratory using the xylydyl blue colourimetric method, with the normal reference range for serum magnesium set at 1.6–2.6 mg/dl. Care was taken to avoid using EDTA, as it can interfere with the results and artificially increase magnesium levels.

Statistical analysis: Data are presented as mean, standard deviation, frequency, and percentage. Continuous variables were compared using an independent-sample t-test. Categorical variables were compared using Pearson's chi-square test. Significance was defined as P values less than 0.05 using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Corp., Armonk, NY, USA).

RESULTS

The mean age of participants in the preterm (25.275 ± 3.875 years) and term (25.133 ± 3.762 years) groups showed no significant difference ($p=0.8144$). The mean BMI between the preterm (23.42 ± 1.868 kg/m²) and term (23.756 ± 2.147 kg/m²) groups also showed no significant difference ($p=0.2926$). The mean gestational age in the preterm group was 32.3 ± 3.004 weeks compared with 38.68 ± 0.725 weeks in the term group, with a significant difference ($p=0.0001$) [Table 1].

Table 1: Comparison of demographics between the groups.

	Preterm	Term	P value
Age (Years)	25.275±3.875	25.133±3.762	0.8144
BMI (Kg/m ²)	23.42±1.868	23.756±2.147	0.2926
Gestation Age (Weeks)	32.3±3.004	38.68±0.725	0.0001

For age distribution, the group aged 21–25 years had the largest proportion in both preterm (46.3%) and term (50.0%) pregnancies, while participants aged >30 years were the least, with 7.5% in preterm and

6.3% in term pregnancies ($p=0.96$). Primigravida participants were more common in both groups, with a higher proportion in the term group (76.3%) than in the preterm group (71.3%) ($p=0.59$).

For the BMI distribution, most participants in both groups had a BMI <25 kg/m² (85.0% in preterm, 81.3% in term), while BMI >25 kg/m² was less frequent (15.0% in preterm, 18.8% in term, p=0.47). Regarding gestational age, preterm pregnancies were predominantly <30 weeks (41.3%) or between 35 and 37 weeks (35.0%), whereas term pregnancies were mostly at 39 weeks (68.8%, p<0.0001). Regarding socioeconomic status, the middle socioeconomic class was the largest group in both

preterm (53.8%) and term pregnancies (61.3%), with the upper class being the least represented (7.5% in preterm pregnancies, 6.3% in term pregnancies, p=0.631). For neonatal morbidity and mortality, preterm neonates had significantly higher rates of respiratory distress syndrome (35.0% vs. 1.3%), jaundice (52.5% vs. 3.8%), and meconium-stained amniotic fluid (21.3% vs. 3.8%) than term neonates. Neonatal mortality occurred only in the preterm group (6.3%; p<0.001) [Table 2].

Table 2: Comparison of demographic and neonatal complications between the groups

		Preterm	Term	P value
Age (Years)	< 20	7(8.8%)	6(7.5%)	0.96
	21-25	37(46.3%)	40(50.0%)	
	26-30	30(37.5%)	29(36.3%)	
	> 30	6(7.5%)	5(6.3%)	
Gravida	Primi	57(71.3%)	61(76.3%)	0.59
	Multi	23(28.8%)	19(23.8%)	
BMI (Kg/m ²)	< 25	68(85.0%)	65(81.3%)	0.47
	> 25	12(15.0%)	15(18.8%)	
Gestation Age (Weeks)	< 30	33(41.3%)	0	<0.0001
	31-34	19(23.8%)	0	
	35-37	28(35.0%)	0	
	38	0	25(31.3%)	
	39	0	55(68.8%)	
Socio-economic Status	Lower	31(38.8%)	26(32.5%)	0.631
	Middle	43(53.8%)	49(61.3%)	
	Upper	6(7.5%)	5(6.3%)	
Neonatal morbidity/ mortality	Respiratory distress syndrome	28(35.0%)	1(1.3%)	<0.001
	Meconium	17(21.3%)	3(3.8%)	
	Jaundice	42(52.5%)	3(3.8%)	
	Intrauterine growth retardation	9(11.3%)	1(1.3%)	
	Death	5(6.3%)	0	

The mean serum magnesium level in the preterm group at <34 weeks (1.031±0.311 mg/dl) compared to >34 weeks (1.293±0.346 mg/dl) showed a significant difference (p<0.001). Similarly, in the

term group, <39 weeks (1.07±0.369 mg/dl) compared to >39 weeks (1.731±0.243 mg/dl) also showed a significant difference (p<0.001) [Table 3].

Table 3: Comparison of serum magnesium levels by gestational age

		Serum magnesium level (mg/dL)	P value
Preterm labor (weeks)	< 34	1.031±0.311	<0.001
	> 34	1.293±0.346	
Term labor (weeks)	< 39	1.07±0.369	<0.001
	> 39	1.731±0.243	

For cervical dilation <3 cm, the mean serum magnesium levels in the preterm group (1.134±0.332 mg/dl) were significantly different from those in the term group (1.587 ± 0.377 mg/dl) (p<0.001). Similarly, in the >3 cm cervical dilation, the mean

serum magnesium levels in the preterm group (0.76±0.4 mg/dl) were compared to the term group (1.497±0.469 mg/dl) also showed a significant difference (p=0.008) [Table 4].

Table 4: Comparison of serum magnesium levels between groups by cervical dilatation

		Serum magnesium level (mg/dL)		P value
		Preterm	Term	
Cervical Dilatation (cm)	< 3	1.134±0.332	1.587±0.377	< 0.001
	> 3	1.076±0.4	1.497±0.469	0.008

DISCUSSION

In our study, the age of the women and parity compared between the two groups showed no significant differences and did not affect the study results, similar to the findings of Kamal et al. The P-value for age distribution is 0.142, which is not

substantial, and the p-value for parity distribution is 0.915, which is also insignificant between both groups.^[2]

In our study, the serum magnesium level was <1.1 in patients in group A, whereas in group B, there were no patients with serum magnesium levels <1.1. Similarly, the study by Malathi et al. shows that the

serum magnesium level is <1.6 in 52% of the patients in Group A, whereas in Group B, there are no patients with serum magnesium <1.6 .^[11]

In our study, the serum magnesium values ranged according to gestational age among patients in group A. There was a low serum magnesium level in early and late preterm patients. However, most patients in the 33-34+6 weeks gestational age group had serum magnesium levels > 2 mg/dL. This may be due to fewer patients belonging to the gestational age group between 33-34+6 weeks of gestation, and further studies might be required to differentiate the serum magnesium level based on gestational age, with no significant difference in the serum magnesium levels among gestation periods. Similar to the study by Vasavi et al., the mean serum magnesium levels in preterm labor patients ranged from 1.47 to 1.59 mg/dl, while term labor patients had levels between 2.08 and 2.81 mg/dl.^[12]

In our study, serum magnesium levels were significantly reduced in preterm labor. Therefore, we demonstrated that the serum magnesium concentration is decreased in preterm labor. Patients in the preterm group had lower serum magnesium levels than those in the full-term gestation group. The mean magnesium was 1.12 ± 0.68 mg/dl for the patients with preterm labor and 1.56 ± 0.82 mg/dl for those with term labor showing a significant difference ($p < 0.001$).

This result is similar to those of other studies. In a study by Pushpo and Jagdish, serum magnesium level in preterm labor was 1.67 ± 0.23 mg/dl.^[13] Kurzel found that the patients with preterm labor had significantly depressed serum magnesium levels, and the mean was 1.60 ± 0.466 mg/dl.^[14] A recent study by Kamal et al. also found that the mean serum magnesium level in preterm labor cases was 1.4 ± 0.22 mg/dl.² It concluded that estimating serum magnesium might be a valuable tool in predicting the preterm onset of labor. Begum et al. also observed a significant reduction ($p < 0.001$) of serum magnesium 1.77 ± 0.36 mg/dl in women with preterm labor.^[15] The studies by Joy et al. and Ferdous et al. show that the mean serum magnesium levels in preterm labor groups ranged from 1.44 to 1.64 mg/dl, while term labor groups had levels between 2.0 and 2.55 mg/dl.^[16,17]

In our study, preterm neonates had significantly higher rates of respiratory distress syndrome, jaundice, and meconium-stained amniotic fluid between the preterm and term groups. Neonatal mortality was observed only in the preterm group. Similar to the study by Molina et al. found that Late preterm infants show higher rates of RDS compared to term infants (55.58% vs. 24.51%, $p < 0.001$), and Preterm infants also experience higher rates of early-onset sepsis (70.59% vs. 35.29%, $p < 0.001$) and longer hospital stays (4.97 vs. 3.55 days, $p = 0.005$).^[18] The study by Berger et al. concludes that RDS in late preterm births is associated with an increased risk of interventricular haemorrhage, retinopathy of prematurity, and sepsis.^[19] Another study by Magno

and Zamora found that Maternal factors such as advanced age and prolonged labor are associated with an increased risk of neonatal respiratory morbidity in meconium-stained labor.^[20]

CONCLUSION

Our study concluded that women experiencing preterm labor had significantly lower magnesium levels than those experiencing term labor. However, no significant differences in serum magnesium levels were observed according to age or parity. These findings confirm that hypomagnesemia can be used as a predictor of preterm labor. Given that the current predictive tests for preterm birth have poor sensitivity and are expensive, magnesium level estimation can be a cost-effective alternative. Magnesium supplementation in patients with reduced serum magnesium levels may help prevent preterm labor and its associated complications such as low birth weight and other adverse pregnancy outcomes.

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