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# Association of Maternal Serum Magnesium Level with Preterm Labour

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**ABSTRACT**

**Background:** Preterm labour is a major health problem in obstetrics. The cause of preterm labour is still unknown. The role of magnesium is also not clear. Recently, involvement of magnesium in physiological and pathological process of labour has been clearly demonstrated.

**Aims and Objectives:** To see the association between maternal scrum magnesium level and preterm labour.

**Materials and Method:** This cross-sectional comparative study was conducted in Department of Obstetrics and Gynecology, Sylhet M.A.G. Osmani Medical College Hospital, between January 2017 and December 2018. Thirty-five pregnant women with preterm labour were selected as case and 35 preterm age and gestational age matched pregnant women without having preterm labour were selected as control group. Serum magnesium concentration was measured.

**Results:** The mean age ($25.43 \pm 4.62$ years versus $24.40 \pm 3.99$ years; p=0.332) and the gestational age ($31.31 \pm 1.78$ weeks versus $31.34 \pm 1.84$ weeks; p=0.974) did not differ between preterm labour group and control group. Serum magnesium level (mg/dl) was significantly lower in prelabour group compared to control group ($0.90 \pm 0.37$ versus $1.69 \pm 0.33$; $p<0.001$).

**Conclusion:** It is strongly suggested that maternal serum magnesium associated with preterm labor of unknown etiology.

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## Introduction

Preterm labour is defined as one where the labour starts before 37th completed weeks (<259 days) counting from 1st day of last menstrual period. The incidence of preterm labour varies between 5 to 10% and the incidence is rising. Preterm labour represents a significant obstetric concern as it is one of the major causes of perinatal and neonatal morbidity and mortality [1]. Preterm birth is responsible for 75% of neonatal death and 50% of long-term morbidity. Preterm infants are at great risk of short term and long-term complication including diabetes mellitus, respiratory disease, impediment in growth and mental development. Preterm birth is responsible for 75% of neonatal death and 50% of long-term morbidity. Hence to predict and prevent the occurrence of preterm labour and delivery would go on a long way to reduce perinatal morbidity and mortality resulting from it [2]. Preterm labour is multifactorial. In about 50% cases the cause is known. Maternal causes are pre-eclampsia, antepartum haemorrhage, premature rupture of membrane, polyhydramnios, cervical incompetence, congenital malformation of uterus, any abdominal operation, high fever, hypertension, diabetes mellitus, nephritis, severe anaemia, low body mass index and genital tract infection like bacterial vaginosis, chlamydial infection. Foetal causes are

multiple pregnancy, congenital malformations, intrauterine foetal death. Placental causes are infarction, thrombosis, placenta previa and abruption. Besides these etiologies preterm labour may be due to biochemical alternation at cellular level stating emphasis to trace elements. Trace elements are not directly attributed in etiology of preterm labour. However, they play an important role in etiopathogenesis of preterm labour, particularly magnesium [3]. Magnesium ($Mg^{+2}$) is the second most abundant intracellular cation [4]. A healthy individual needs to ingest 4.5 mg/kg body weight/day to stay in balance magnesium level [5]. The daily requirement is higher during pungency and it is about 400 mg/day (under 19 years), 350mg/day (19 years to 30 years), 360 mg/day (31 years and above). Serum magnesium decrease during pregnancy and may be responsible for decrease of magnesium in myometrium leading to uterine irritability by its inhibition of adenyl cyclase which results in increase in cytoplasmic calcium level [6]. This increase in calcium increases neuromuscular conduction leading to uterine hyperactivity and cervical dilatation which in turn facilitates labour [3]. Since magnesium has an inhibitory role on myometrial contractions, attention has been paid to the role of magnesium deficiency in causing preterm labour with unknown etiology where uterine contractions begins with hypomagnesaemia [7]. A Number of previous studies found a correlation between level of maternal magnesium reduction and preterm labour [8]. Some other studies found no relationship between the two variables [4, 5, 7, 9-11]. However, due to the paucity of data in this regard in North-East part of Bangladesh, this study therefore aimed to investigate whether low maternal serum magnesium during pregnancy associated with preterm labour and there after described framework for combining this screening information with designing a prophylactic intervention [12-15].

## Materials and Methods
This cross-sectional comparative study was carried out in the Department of Obstetrics and Gynecology, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet berween January 2017 and December 2018. Thirty five pregnant women with preterm labour (between 28 weeks and 36+6 weeks of gestational age, regular uterine contraction: at least one in every 10 minutes for ≥ 4 hours, intact fetal membrane, cervical effacement: ≥ 80%, dilation of Cervix ≥ 2 cm) and aged between 18 years and 40 years were selected as Group-I (premature labour group) and 35 age and gestational age matched pregnant women without having preterm labour were selected as Group-II (control group). Exclusion criteria were (1) patients with medical disorder like Heart block, chronic kidney diseases, Diabetes mellitus, Hypertension and presence of genito-urinary infection; (b) patients with obObstetrical disorder such as Preeclampsia, Eclampsia, Multiple pregnancy,APH Antepartum haemorrhage, Polyhydramnios,Intruterine foetal death, Congenital fetal anomalies, cervical incompetence, Uterine malformation and PROM; (3) patients were on Proton pump inhibitors, Loop and thiazide diuretics and aminoglycoside, gentamycin etc; and .(4) those who refused to enroll in study.

After admission of pregnant women with preterm labour, history was taken, and clinical examination was done. A patient was said to be in preterm labour if she presented with the following: (1). Contractions of 4 in 20 minutes or 8 in 60 minutes plus progressive cervical changes (2). Cervical dilatation greater than 1 cm (3) Cervical effacement of 80% or greater [16].

Selection criteria were applied. Those who fulfilled inclusion criteria were enrolled in this study. In this way 35 pregnant women with preterm labour (without any known etiology) were selected as case and 35 preterm age and gestational age matched pregnant women without having preterm labour were selected as control group.

## Method of Collection of Samples for Estimation of Serum Magnesium Levels
After obtaining informed written consent and with all aseptic precaution 3ml venous blood sample was collected in disposable syringe from anticubital vein without any anticoagulant. Then the sample was sent to the Department of Biochemistry, Sylhet M.A.G. Osmani Medical College for estimation of serum $Mg^{+2}$ level. The quantitative assessment-of serum $Mg^{+2}$ level was done on INDIKO auto analyzer using a magnesium reagent kit by photochromatic method.

## Data Analysis
All collected data were compiled and analyzed using the statistical Package for social Science (SPSS) Version 22.0. Quantitative data were expressed as mean and standard deviation (SD); and comparison between two groups using unpaired t test. Qualitative data were expressed as frequency and percentage; and comparison was done using chi-squre test ($\chi$2) or Fisher's Exact-test where appropriate. A probability value (p) of less than 0.05 was considered statistically significant.

## Results
The mean age of the participants was $25.43 \pm 4.62$ years (range 18 to 35 years) in preterm labour and was $24.40 \pm 3.99$ years (range 18 to 35 years) in control group. There was no significant different of mean age between two groups (t=0.997; p=0.332) (Table:1).

**Table I: Distribution of the Participants according to Age**

| Age | Group-I (n=35) | Group-II (n=35) | p-value |
|---|---|---|---|
| ≤20 years | 6 (17.1%) | 5 (14.3%) | |
| 21-25 years | 12 (34.3%) | 18 (51.4%) | †p=0.466 |
| 26-30 years | 12 (34.3%) | 10 (28.6%) | |
| 31-35 years | 5 (14.3%) | 2 (5.7%) | |
| Mean ± SD | 25.43 ± 4.62 | 24.40 ± 3.99 | *p=0.332 |

According to obstetrical history of gestational age, parity and miscarriage, no statistically significant difference was observed between the two groups (p=0.974, p=0.329 and p=0495) (Table:2).

**Table 2: Obstetrical History in Both Groups**

| Variables | Group-I (n=35) | Group-II (n=35) | p-value |
|---|---|---|---|
| **Gestational age** | | | |
| 28-30 weeks | 15 (42.9%) | 15 (42.9%) | †p=1.000 |
| 31-33 weeks | 16 (45.7%) | 15 (42.9%) | |
| 34-36 weeks | 4 (11.4%) | 5 (14.3%) | |
| Mean (SD) | 31.31 ± 1.78 | 31.34 ± 1.84 | *p=0.974 |
| **Parity** | | | |
| Nulliparity | 19 (54.3%) | 23 (65.7%) | *p=0.329 |
| 1 or more | 16 (45.7%) | 12 (34.3%) | |
| **Miscarriage** | | | |
| Yes | 6 (17.1%) | 4 (11.4%) | *p=0.495 |
| No | 29 (82.9%) | 31 (88.6%) | |

There was no significant difference in employment status (p=0.205) while for socioeconomic classes, there was statistically significant difference between two groups (p=0.387) depicted in Table:3.

**Table 3: Social Characteristics in Both Groups**

| Variables | Group-I (n=35) | Group-II (n=35) | p-value |
|---|---|---|---|
| **Socioeconomic Status** | | | |
| Rich class | 0 (0.0%) | 0 (0.0%) | p=0.387 |
| Upper middle class | 7 (20.0%) | 3 (8.6%) | |
| Lower middle class | 19 (54.3%) | 21 (60.0%) | |
| Lower class | 9 (25.7%) | 11 (31.4%) | |
| **Employment status** | | | |
| Housewife | 27 (77.1%) | 31 (88.6%) | p=0.205 |
| Employed | 8 (22.9%) | 4 (11.4%) | |

The mean serum magnesium level (mg/dl) in preterm labour group was $0.90 \pm 0.37$ and was as $1.69 \pm 0.33$ in control group. Serum magnesium level was significantly lower in preterm labour group compared to control group (t=-9.465; p<0.001) (Figure:1).
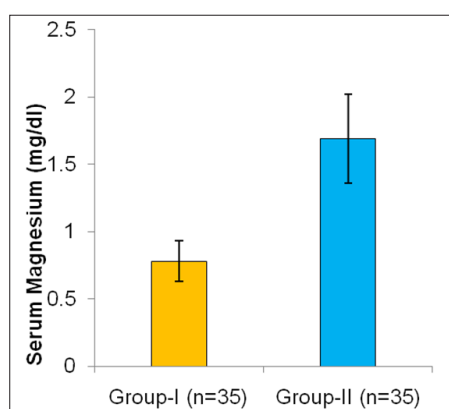


**Figure 1:** Distribution of the Participants according to Serum Magnesium Level
Group-I = Preterm Labour; Group-II = Control

The mean serum magnesium level (mg/dl) was significantly lower in preterm labour group compared to control group in the gestational age group of 28-30 weeks ($0.77 \pm 0.12$ versus $1.73 \pm 0.31$; t=-11.129; p<0.001); in the gestational age group of 31-33 weeks ($0.78 \pm 0.19$ versus $1.65 \pm 0.35$; t=-8.728; p<0.001); and group in the gestational age group of 34-36 weeks ($0.82 \pm 0.04$ versus $1.66 \pm 0.39$; t=-4.206; p=0.004) (Figure:2).
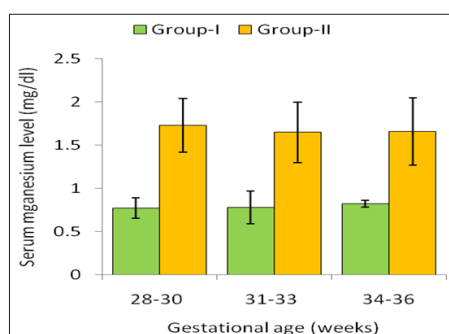


**Figure 2:** Serum Magnesium levels at different Gestational Age

**Discussion**

Preterm birth is a major cause of neonatal mortality with the highest rates of health care costs due to hospitalization of woman with preterm labour and the expenses of long-term care of preterm birth. In addition, prevention of disabilities due to preterm birth is very important for the Neonatalogists. During the recent years, concerning the related causes and early prediction of preterm labour has increased significantly [10]. A number of previous studies found a correlation between level of maternal serum magnesium reduction and preterm labour [17]. Some other studies found no relationship between the two variables [9, 11, 18- 19]. Considering a few literatures and controversies on correlation between serum magnesium level and preterm labour, this study was conducted to compare the serum magnesium level in preterm labour and in those who had a similar gestational age but delivery at term [12-15]. In this study the mean age of the participants of preterm labour was $25.43 \pm 4.62$ years and of term labour was $24.40 \pm 3.99$ years. There was no significant different of mean age between two groups (p=0.332). This result correlated with several studies. This study also revealed that 68.6% patients were aged between 21 to 30 years, 17.1% patients were up to 20 years and 14.3% patients were between 31 to 35 years in preterm labour group; whereas 80.0%, 14.3% and 5.7% respectively in control group; difference was not statistically significant (p=0.466). Begum and Das, found similar age distribution of the pregnant women [4, 7, 10, 19]. In this study 54.3% of women were primi-parous in preterm labour group and 45.7% women were multi-parous; whereas in 65.7% women were primi-parous and 34.3% women were multi-parous in preterm comparator group. There was significant difference of parity between two groups (p=0.329). This result was supported by Khani et al. supported this finding. But other study revealed 35.0% of women were nulliparous in preterm labour group [10]. In the present study 17.1% women had history of miscarriage in preterm labour group and 11.4% women had history of miscarriage in preterm comparator group [4]. There was no significant difference of miscarriage between two groups (p=0.495). This result was almost similar to the study several studies. This study revealed that the most frequent socioeconomic status was lower middle class in both preterm labour group (54.3%) and preterm comparator group (60.0%) followed by lower class (25.7%) versus (31.4%) and upper middle class (20.0%) versus (8.6%). There was no significant difference of socioeconomic classes between two groups (p=0.387) [4, 10, 11, 20, 21]. This result was consistent with several studies. This result reflects the real figure in our society, as the lower social class women attend governmental hospital because they could not bear the cost in the private hospitals [10, 11, 20]. In the present study the most frequent employment status was house wife in both preterm labour group (77.1%) and preterm comparator group (88.6%); while employed was 22.9% and 11.4% respectively. There was no significant difference in employment status between two groups (p=0.205). This was supported by other studies. In this study the mean serum magnesium level of the participants was $0.90 \pm 0.37$ mg/dl in preterm labour group and was $1.69 \pm 0.33$ mg/dl in preterm comparator group [4, 10, 21]. Serum magnesium level was significantly lower in preterm labour group compared to preterm comparator group (p<0.001). Similar findings were reported by in several studies. But several other studies revealed no relationship between maternal serum magnesium level and preterm labour [5, 7, 9, 11, 18-20, 22]. In the present study the mean serum magnesium level (mg/dl) was significantly lower in preterm labour group compared to control group in the gestational age group of 28-30 weeks ($0.77 \pm 0.12$ versus $1.73 \pm 0.31$; p<0.001); in the gestational age group of 31-33 weeks ($0.78 \pm 0.19$ versus $1.65 \pm 0.35$; p<0.001); and group in the gestational age group of 34-36 weeks ($0.82 \pm 0.04$ versus

$1.66 \pm 0.39$; p=0.004) [12-15]. This result correlated with other studies. The exact mechanism of action of Magnesium is not understood. Calcium by its action on calmodulin activation brings about uterine contraction, while Magnesium prevents it [4, 23]. The serum Magnesium level may affect the blood flow through the uterus and may contribute towards lysosome stabilization. The stabilization of which brings about release of prostaglandins which initiates contractions. The following limitation faced during this study (1) this study was conducted in a tertiary care hospital, (2) sample size was small and (3) sampling was non-probability convenient sampling [22].

## Conclusion
It may be concluded that that maternal serum magnesium is associated with preterm labour of unknown etiology. Estimation of serum magnesium levels may be a useful parameter in pregnancy especially in women at high risk of preterm labour. However further study involving multicentre and large sample should be conducted to evaluate the role of magnesium in the occurrence of preterm labour.

## Author's Contribution
Mahnaz Syed designed the study and collected the data; Md. Ziaur Rahman designed the study and drafted the manuscript; Md. Tabibul Islam analysed and interpreted the data and critically reviewed the manuscript; Dilip Kumar Bhowmik supervised the study; Hasina Choudhury, Mubraka Faizah, Masuma Khan and Md. Bahauddin critically reviewed the manuscript. Approval of final manuscript was by all authors.

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**Conflict of interest:** None declared.

## Ethical Issue
- Informed written consent was taken from each of patient and
- An approval of the study was obtained from the Institutional Ethics Committee of Sylhet M.A.G Osmani Medical College, Sylhet, Bangladesh.

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