

## Low Serum Magnesium in Preterm Labour

AA BEGUM<sup>a</sup>, TR DAS<sup>b</sup>

### Summary:

*This study was designed to compare serum magnesium level in women with preterm labour and with those who were in term labour.*

*A case-control study was carried out in the department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from July 2005 to June 2007, to evaluate serum magnesium level in women with preterm labour (28-36 weeks) and compare them with those who were in term labour (37-40 weeks). The total number of cases was 160, of which 80 were cases and similar number were control.*

*The study subjects were selected from inpatient department of Obstetrics and Gynaecology, BSMMU and Mother and Child Health Training Institute (MCHTI), Dhaka.*

*Serum magnesium level was measured by taking 5 ml of blood from women with term (control) and preterm labour (case).*

*The basic characteristics, like age, parity and socioeconomic status did not show statistically any significant difference between control and case groups, but showed significant difference only in the body mass index between the two groups. Mean ( $\pm$ SD) BMI in control and case groups were  $24.88\pm 1.42$  and  $23.12\pm 2.36$  kg/m<sup>2</sup> respectively.*

*Mean ( $\pm$ SD) gestational age were  $38.95\pm 0.89$  and  $33.03\pm 1.83$  weeks, respectively in control and case groups.*

*The mean ( $\pm$ SD) serum magnesium levels were  $2.02\pm 0.20$  (range 1.70-2.4) and  $1.65\pm 0.19$  (range 1.30-2.00) mg/dl, respectively, in control and case groups. 'The difference was highly significant ( $p<0.001$ ).*

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### Introduction:

Preterm labour is defined as labour occurring before 37 completed weeks of gestation.<sup>1</sup> Preterm labour with its complications is the leading cause of perinatal mortality and morbidity and poses a great challenge to modern obstetrics. Incidence of preterm labour varies between 5 and 10 percent, and is related to socioeconomic status, disease pattern, genetic constitution and geographic locations.<sup>2,3</sup>

Preterm labour is associated with many obstetric, medical and anatomical disorders. But the cause of preterm labour in 50 percent of pregnancies, however, is idiopathic.<sup>4</sup> Some important risk factors are severe hypertensive disorder, premature rupture of membrane (PROM), polyhydramnios, low socioeconomic status, low gynecologic age, renal disease, heart disease and

previous cervical injury. Besides various aetiology, it may be due to alteration in basic biochemical functions of the body at cellular level stating emphasis to trace elements, of which magnesium being one of them, is subject of interest nowadays.<sup>5</sup> Normally, basic biochemical functions of the body are maintained by various minerals, water and trace elements. Magnesium, one of the trace elements, is an important cation of the body. It was shown that low magnesium plays a vital role in the premature onset of labour.<sup>6</sup>

Decrease of magnesium plays an important role in the physiology of parturition. Decrease of magnesium in plasma may be responsible for decrease of the same in myometrium, and this might have a considerable influence on preterm labour, thus suggesting the prophylactic administration of magnesium in pregnancy to be useful.<sup>7</sup>

Rising serum magnesium level serves to relax uterine smooth muscles, thereby providing the basis for the use of magnesium sulphate as a tocolytic agent.<sup>8</sup>

Magnesium is inexpensive and well-tolerated when given to patient in preterm labour. Many pregnant women, particularly women of lower socioeconomic status, do not have adequate magnesium in their diet.<sup>6</sup>

a. Dr. Anzuman Ara Begum, Junior Consultant, Obs & Gynae Department, Dhaka Medical College Hospital, Dhaka.

b. Dr. Tripti Rani Das, Associate Professor, Obs & Gynae Department, Bangabandhu Sheikh Mujib Medical University, Dhaka.

**Address of Correspondence:** Dr. Anzuman Ara Begum, Junior Consultant, Obs & Gynae Department, Dhaka Medical College Hospital, Dhaka.

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Magnesium and calcium, similar to sodium and potassium, plays an important role in the physiology of contraction of smooth muscle. Magnesium, which antagonizes the action of calcium, is successfully employed in the preventive treatment of preterm labour. Physiology and pathophysiology of magnesium are the subject of current research in obstetrics. Magnesium activates approximately 200 enzymes and affects the nerve conduction and uterine contractility. The decreased serum concentration of total calcium and magnesium in women with threatening of preterm delivery may be related to premature uterine contractility. Possible mechanism by which hypomagnesaemia induces uterine irritability is by inhibition of adenylyl-cyclase with resultant increase in cytoplasmic calcium level. Hypomagnesemia may be a marker of preterm labour.<sup>9</sup>

Thirteen percent of all infants are classified as low birth weight (<2.5 kg). Three percent of these are mature low-birth-weight infants and about 10 percent are truly premature. The latter group accounts for nearly two-thirds of infant deaths (approximately 25,000 annually in the United States).<sup>4</sup>

The care of premature (birth weight 1.0-2.5 kg) and immature (birth weight < 1 kg) infants is costly. Compared with term infants, those born prematurely suffer from greatly increased morbidity and mortality (e.g. functional disorders, abnormalities of growth and development). Thus, every effort should be made to prevent or inhibit premature labour.<sup>4</sup>

The aim of this study is to determine the relationship between serum magnesium level and preterm delivery, so that the high morbidity and mortality related to prematurity could be reduced by early diagnosis of this deficiency and its correction.

#### **Materials And Methods:**

This was a case control study carried out in the department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Maternity and Child Health Training Institute (MCHTI) during the period from July 2005 to June 2007.

Total 160 pregnant women aged 16 to 40 years of whom 80 at term (between 37 and 40 weeks gestation), singleton pregnancy with regular uterine contraction at a frequent interval documented by uterine palpation,

generally more than two in 30 minutes with dilatation (at least 2 cm) and effacement of cervix were enrolled in this study. Study subjects were selected from admitted patients, department of Obstetrics and Gynaecology, BSMMU and MCHTI, Azimpur, Dhaka.

#### **Inclusion criteria**

##### **Control**

- a) Pregnant women aged 16-40 years
- b) Singleton pregnancy
- c) After 37 completed weeks of gestation with labour pain

##### **Case**

- a) Pregnant women aged 16-40 years
- b) Singleton pregnancy
- c) Gestation age between 28 and 36 weeks
- d) Painful uterine contraction more than two in 30 minutes
- e) Dilatation (at least 2 cm) and effacement of cervix

#### **Exclusion criteria**

##### **Control**

- a) Pregnant women having any major disease, such as diabetes, preeclampsia/eclampsia
- b) History of taking prior tocolytic agents
- c) Placenta praevia

##### **Case**

- a) Women having any known factor of premature labour like,
  - pregnancy with fibroid uterus
  - pregnancy with known hypoplastic uterus or other uterine abnormalities
- b) Prior tocolysis
- c) Multiple pregnancy
- d) Ruptured membrane
- e) Placenta praevia
- f) Incompetent cervix
- g) Known or detected fetal abnormality
- h) Polyhydramnios

#### **Study Procedure**

In this study, serum magnesium level of a group of women with term and preterm labour pain was estimated and compared.

Blood was collected from antecubital vein of the control and case groups with disposable syringe with full aseptic precaution. Blood was drawn once from each subject. Collected blood samples were kept in 5 ml screw-capped vials. After collection of blood samples, these were immediately brought to the Department of Biochemistry, BSMMU, where serum was separated by centrifugation (at 3000 rpm, at 20°C, for 10 minutes). These serum samples were then analyzed for serum magnesium level by special magnesium analysis kit.

### Results:

Among 160 study group 80 control 80 case, of them mean ( $\pm$ SD) age in control and case groups, respectively were 26.05 $\pm$ 5.13 and 25.68 $\pm$ 5.84 years (range 18-37 and 17-36 years). Age did not show any significant difference between the two study groups (Table-I).

Table-II shows significant difference in BMI between control and case group. Mean ( $\pm$ SD) BMI in control group was 24.88 $\pm$ 1.42 and in case group was 23.12 $\pm$ 2.36 kg/m<sup>2</sup>. BMI  $\leq$  25 kg/m<sup>2</sup> in control group was seen in 38(47.5%) and in case group in 52(65%) women while BMI >25 kg/m<sup>2</sup> was seen in 42(52.5%) of control and 28(35%) of case group of women.

Table-III shows what serum magnesium level was significantly low in case group of women (mean $\pm$ SD 1.65 $\pm$ 10.19, range 1.30-2.00 mg/dl) compared to control group of women (mean $\pm$ SD 2.02 $\pm$ 0.20, range 1.70-2.40 gm/dl).

Effect of socioeconomic status on serum magnesium level in control group shows significant difference in serum magnesium level between low and middle income groups ( $p < 0.01$ ), while in case group, there was no significant difference. In both the groups (control and case), mean serum magnesium level was higher in middle-income group of women compared to low-income group Table-IV.

Table-V shows the effect of BMI (Body Mass Index) on serum magnesium levels in control and case group. In control group, BMI showed significant difference in serum magnesium level between  $\leq$  25 kg/m<sup>2</sup> and >25 kg/m<sup>2</sup> groups ( $p < 0.01$ ), while in case group, there was no significant difference. In both the groups (control and case), mean serum magnesium level was higher in women with BMI >25 kg/m<sup>2</sup> compared to  $\leq$  25 kg/m<sup>2</sup>.

**Table-I**

<i>Age distribution of the study subjects</i>					
Age (years)	Control (n=80)		Case (n=80)		p value
	No.	(%)	No.	(%)	
$\leq 25$	34	(42.5)	40	(50.0)	> 0.10 <sup>NS</sup>
26-30	34	(42.5)	22	(27.5)	
>30	12	(15.0)	18	(22.5)	
Mean $\pm$ SD	26.05 $\pm$ 5.13		25.68 $\pm$ 5.84		> 0.50 <sup>NS</sup>
Range	18-37		17-36		

Chi-square test/Unpaired Student's 't' test

<sup>NS</sup>=Not significant

**Table-II**

<i>Body mass index of the study subjects</i>					
BMI (kg/m <sup>2</sup> )	Control (n=80)		Case (n=80)		p value
	No.	(%)	No.	(%)	
$\leq 25$	38	(47.5)	52	(65.0)	< 0.05*
> 25	42	(52.5)	28	(35.0)	
Mean $\pm$ SD	24.88 $\pm$ 1.42		23.12 $\pm$ 2.36		< 0.001***
Range	20.89-27.06		17.31-27.41		

Chi-square test/Unpaired Student's 't' test

<sup>NS</sup>=Not significant \* = Significant

**Table-III**

<i>Comparison of serum magnesium level</i>			
Serum magnesium(mg/dl)	Control (n=80)	Case (n=80)	p value
Mean±SD	2.02±0.20	1.65±0.19	>0.001***
Range	1.70-2.40	1.30-2.00	

Unpaired Student's 't' test

\*\*\*=Significant

**Table-IV**

<i>Effect of socioeconomic status on serum magnesium level</i>			
Socioeconomic status	Serum magnesium (mg/dl)		p value
	Control	Case	
Low			
Mean±SD	1.92±0.13	1.61±0.17	< 0.001***
Range	1.70-2.20	1.30-1.90	
n	24	32	
Middle			
Mean±SD	2.06±0.21	1.67±0.19	< 0.001***
Range	1.70-2.40	1.40-2.00	
n	56	48	
p value	<0.01**	>0.10 <sup>NS</sup>	

Unpaired Student's 't' test NS=Not significant \*\*/\*\*=Significant

**Table-V**

<i>Effect of BMI on serum magnesium level</i>			
BMI (kg/m <sup>2</sup> )	Serum magnesium (mg/dl)		p value
	Control	Case	
≤ 25			
Mean±SD	1.95±0.16	1.62±0.17	< 0.001***
Range	1.70-2.40	1.30-1.90	
n	38	52	
> 25			
Mean±SD	2.08±0.21	1.69±0.21	< 0.001***
Range	1.70-2.40	1.40-2.00	
n	42	28	
p value	<0.01**	>0.10 <sup>NS</sup>	

Unpaired Student's 't' test NS=Not significant \*\*/\*\*=Significant

**Discussion:**

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. In the present

study, serum magnesium level was estimated in 80 cases of preterm labour and in 80 controls of normal term labour. Serum magnesium level was significantly low in preterm group of women (mean±SD 1.65±0.19, range 1.30-2.00 mg/dl) compared to term group of women

(mean±SD 2.02±0.20, range 1.70-2.40 mg/dl). Hence, hypomagnesaemia may be a risk factor in cases of pregnancy where it may result in preterm labour.

In the present study, no significant difference in age, parity and socioeconomic status between control and case groups was observed. There was significant difference in body mass index (BMI). Though there was a relationship between low socioeconomic status, i.e. poor nutrition with preterm labour, in this study it was found that most of the women from control (70%) and case (60%) groups belonged to middle socioeconomic group. Women from higher socioeconomic class usually do not attend BSMMU hospital and MCHTI. The number of low socioeconomic group of pregnant women was also less in BSMMU hospital.

A study showed low serum magnesium level in preterm labour cases. In their study, serum magnesium level was also found to be low in patients belonging to low socioeconomic status, thus relating the low level of magnesium to diet deficient in magnesium.<sup>10</sup>

In a study the serum magnesium level was found to be significantly lower in preterm labour patients than in nonpregnant and normal pregnant women. In the same study mean (±SD) serum magnesium level in preterm labour cases was 1.42±0.22 mg/dl. In 15 cases of second trimester preterm labour, mean (±SD) serum magnesium level was found to be 1.55±0.24 mg/dl. The mean (±SD) serum magnesium level was 1.37±0.19 mg/dl in third trimester preterm labour cases. No significant influence of age and parity was found on serum magnesium levels.<sup>6</sup> In present study no significant influence of age and parity was found.

The findings of the present study also demonstrated that serum magnesium concentration was lower in preterm labour, which was 1.65±0.19 (range 1.70-2.40 mg/dl). It was considered serum magnesium level below 1.8 mg/dl as hypomagnesaemia which may lead to preterm labour. It was found that labour was prolonged when magnesium sulphate was used in eclamptic patients.<sup>11</sup> It was demonstrated that magnesium sulphate is effective as primary tocolytic agent with minimal side-effect. The average level of magnesium in nonpregnant healthy women of reproductive age is 2.40.49 mg/dl.<sup>12</sup>

A study reported serum magnesium level ranged in nonpregnant women 1.8-2.8 mg/dl (mean±SD 2.2±0.33 mg/dl), in normal pregnant women 1.5-2.4 mg/dl

(mean±SD 1.9±0.3 mg/dl) and in women with preterm labour 0.96-1.80 mg/dl (mean±SD 1.47±0.33 mg/dl). The difference was significant ( $p<0.001$ ) when compared between normal pregnant women and women with preterm labour.<sup>10</sup>

In a study it was found that serum magnesium level in preterm labour was 1.60±0.46 mg/dl.<sup>13</sup> In a study serum magnesium level was 1.67±0.23 mg/dl.<sup>6</sup> In two other studies, the serum magnesium level in preterm labour were 1.64±0.07 mg/dl and 1.63±0.053 mg/dl, respectively.<sup>14,15</sup>

A study in our country found serum magnesium level in preterm labour as 1.77±0.36 mg/dl.<sup>16</sup> In this study, serum magnesium level was found as 1.65±0.19 mg/dl, in preterm labour which was also significantly low.

All the above studies showed that hypomagnesaemia may be a risk factor for preterm labour.

In an epidemiologic study it was demonstrated that prophylactic oral magnesium supplementation to patient at risk for preterm labour was successful in lowering the preterm delivery rate. Prevention of preterm labour by intake of magnesium should be sufficient to maintain serum magnesium level at the range of 2.0-3.5 mg/dl.<sup>17</sup>

In this study, among the women with preterm labour (28-36 weeks of gestation), statistically, significant lower level of serum magnesium was observed. The lower serum magnesium level, therefore, reflected the tendency of preterm labour or initiation of preterm labour. Therefore, a role of magnesium in the pathophysiology of preterm labour is strongly suspected. Whether magnesium levels drops preceding the development of preterm labour is unknown. Hypomagnesaemia, therefore, may be either a causative factor or simply reflect the process involved with the development of uterine irritability in preterm labour.

#### **Conclusion:**

From the present study, it may be concluded that:

- Serum magnesium level was significantly low in women having preterm labour
- Serum magnesium level was significantly lower in low BMI (body mass index) group of women
- No significant difference in serum magnesium level with age and parity was observed

It may be concluded that estimation of serum magnesium in pregnancy may prove to be a valuable tool in predicting preterm onset of labour. The results of the present study add to the existing evidence that low serum magnesium level may be a risk factor for preterm labour.

### Recommendation:

Further study is needed with large sample size.

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