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Original Research Article

Study on Association of Serum Magnesium with Preterm Labour

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Abstract

Background: Magnesium plays an import role in the physiology of parturition. Decrease of Magnesium in plasma may be responsible for a decrease of the same in myometrium and this might have a considerable influence on the preterm labour. A Hypomagnesaemia leads to neuromuscular irritability leading to uterine hyperactivity which leads to cervical dilation. ***Objective:*** To find out the association between serum magnesium and preterm level. ***Methods:*** This was a cross sectional study, conducted in 100 women in labour, of them 50 were diagnosed case of preterm labour and 50 women were in labour at term attended in Gynaecology and Obstetrics department of Dhaka Medical College, Dhaka, from January 2015 to December 2015.5ml fasting blood sample was collected and was analyzed for serum magnesium using a standard enzymatic method. The mean value of serum magnesium was compared between two groups by student unpaired t-test and serum magnesium level was correlated with BMI, Gravita and gestational age in preterm labour patients by Pearson's correlation coefficient test. A p-value was considered to be statistically significant at 0.05 at a 95% confidence interval. ***Results:*** The mean age was found 28.2±4.5 years in group I and 26.7±4.1 years in group II. The mean age difference was not statistically significant ($p>0.05$) between two groups. A majority (80.0%) of the patients came from a middle-class family in group I and 29(58.0%) in group II. The mean BMI was found 23.0±3.8 kg/m^2 in group I and 26.4±2.4 kg/m^2 in group II. The socioeconomic status and BMI were statistically significant ($p<0.05$) between two groups. The mean serum magnesium was found 1.64±0.13 mg/dl in group I and 2.05±0.11 mg/dl in group II. The mean serum magnesium level was significantly ($p<0.05$) lesser in group I. Serum magnesium had an area under curve 0.974, which gave a cut-off value < 1.8 mg/dl, with 98.0% sensitivity and 88.0% specificity for prediction of preterm labour. ***Conclusion:*** Most of the patients were belonged to age 21-30 years in both groups are not associated. A negligible correlation was found with BMI, gravid, through serum magnesium in preterm labour. Low serum magnesium level was significantly higher in preterm labour.

Keywords: Magnesium, Physiology of parturition, Preterm labour, Term labour, Hypomagnesaemia, neuromuscular irritability.

INTRODUCTION

Causing progressive cervical changes before 37 completed weeks of gestation preterm labour is defined as labour occurs with regular and frequent uterine contractions. Almost ten percent (9.6%) of all births were preterm estimated by Beck *et al*., [1]. The vast majority (85.0%) of global preterm births occur in Asia and Africa, where health systems are weak and inadequate [1, 2]. The regions with the highest preterm birth rates in 2010 were Southeastern Asia 13.3% followed by Sub-Saharan Africa 12.3% and Developed

countries 8.6%. More than 60.0% of all preterm births are estimated to have occurred in sub-Saharan Africa and South Asia where 12.8% of live births were estimated to be preterm in 2010. In 2013, the preterm birth rate in Germany, Brazil and United States were 8.7%, 10.7% and 12.0%, respectively [3, 4]. The highest live preterm birth rate was in Pakistan 15.8% followed by Indonesia 15.5%, Philippines 14.9%, Bangladesh 14.0%, Indian at 13.0%, Nigeria 12.0% and 9.2% in Brazil [5]. Although the path physiology of preterm labour remains incompletely defined, a growing body of evidence is emerging that links occult upper genital tract infection with subsequent spontaneous preterm labour. Pathogenesis of preterm labour is not also understood but preterm labour might represent early idiopathic activation of normal labour process. An important pathway leading to labour initiation implicates inflammatory decidual activation and in many cases of preterm labour, decidual activation seems to arise in the context of intra-uterine bleeding or an occult intrauterine infection [6]. Risk factors for preterm birth include demographic characteristics, behavioral factors, and aspects of obstetric history such as previous preterm birth. Demographic factors for preterm labor include nonwhite race, extremes of maternal age (under 17 years or more than 35 years), low socioeconomic status, and low prepregnancy weight. Preterm labor and birth can be associated with stressful life situations like domestic violence; close family death; insecurity over food, home, or partner; work and home environment either indirectly by associated risk behaviours or directly by mechanisms not completely understood. In the same gravida many risk factors may manifest [7]. It is known that serum magnesium levels fall during pregnancy with gestational age. This decrease of magnesium plays an important role in the physiology of parturition. Resulting in muscle cramps and uterine hyperactivity hypomagnesemia leads to neuromuscular hyperexcitability. By hypomagnesemia leads to increased cervical dilatation which in turn facilitates approach of vaginal micro-organisms into cervical canal, hyperexcitability of uterine musculature induced. While uterine passage is being colonized by pathogenic micro-organisms it changes quality and quantity of vaginal discharge [8]. For the offspring and for the mother preterm delivery is not only a leading cause, its long-term sequelae pose a serious problem of neonatal morbidity and mortality [9]. Preterm labor complicates 10-15% of all pregnancies and is the number one cause of neonatal morbidity and mortality and causes 75% of neonatal deaths that are not due to congenital anomalies [10]. Compared with term infants, those born prematurely suffer from greatly increased morbidity and mortality like as abnormalities of growth and development and functional disorders. Therefore, every effort should be made to prevent or inhibit premature labour [11]. In Bangladesh, preterm labor considered as a health hazard both for mother and child. Most of our pregnant women have a poor health condition. They are also lying face down to develop infection and there by susceptible to various morbidities even to mortality (e.g. puerperal sepsis, Chorioamnionitis etc.). So inadequate obstetric care at the time of delivery further magnifies the problem. Identification of the vulnerable group of women will help to design a strategy for early detection and management of preterm labor and reduce the perinatal morbidity and mortality and also the maternal complications. As the etiology of preterm labour is multifactorial, the attempts to predict it are not very successful and accurate. However, due to the paucity of data in this regard in our country, this study will therefore aim to investigate whether low maternal serum magnesium during pregnancy may be associated with preterm labour and delivery in the Bangladeshi pregnant population. By early diagnosis of this deficiency and its correction, the high morbidity and mortality related to prematurity could be reduced. Thereafter describe a generic framework for combining this screening information with designing a prophylactic intervention.

OBJECTIVES OF THE STUDY

General:

To find out the association of hypomagnesemia with preterm labour.

Specific:

- To estimate serum magnesium level among preterm labour and women in term labour.
- To compare the level of serum magnesium between women in preterm labour and women in term labour.
- To find out the association between serum magnesium and women in preterm labour.

METHODOLOGY

This was an observational type of study with cross sectional design by using the Purposive sampling method. The target patient was Pregnant women with 28-40 wks of gestation. 100 sample was covered. 50 in each group. Group 1 (50 women in preterm labour) and Group II (50 women in term labour). The study period was from July 2014 to June 2015 at the department of Obstetrics & Gynaecology, Dhaka Medical College Hospital (DMCH), Dhaka.

Data collection procedure

Data was collected using a structured questionnaire containing all the variables of interest and by interview, clinical examination and laboratory investigations and data were recorded on the pre-designed data collection sheet. Data collection sheet is attached as Appendix-II. Samples were collected from the inpatient Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka. The purpose and procedure of the study were discussed with the patients who fulfilled the inclusion criteria. Written consent was taken from those who agreed to be

included in the study. A consent form is attached as Appendix-III.

Statistical analysis

After editing and coding, the coded data were directly entered into the computer by using the software SPSS version 20.0. Results were expressed as mean + SD for continuous data. By unpaired student t-test, mean values were compared. For all analytical tests, the level of significance was $p < 0.05$ considered significant at a 95% confidence interval.

Ethical consideration

Prior permission was taken from Ethical Review Committee (ERC), Dhaka Medical College (DMCH) Hospital, Dhaka to undertake this study. Keeping compliance with Helsinki Declaration for Medical Research Involving Human Subjects 1964, all the study subjects was informed verbally about the study design, the purpose of the study and potential benefits for the community. Patients with term and preterm labour who has informed consent to participate in the study was included in the study sample.

RESULTS

Table I: Distribution of the study patients by socio-demographic variables, (N=100)

Socio-demographic variables	Group I (Preterm) (n=50)		Group II (Term) (n=50)		P- value
	n	%	n	%	
Age (In year)					
≤20 yrs.	0	0.0	1	2.0	
21 - 30 yrs.	34	68.0	39	78.0	
31 - 40 yrs.	16	32.0	10	20.0	
Mean ±SD	28.2±4.5		26.7±4.1		[a]0.085[ns]
Range (min, max)	21- 36		20-35		
Socioeconomic status					
Lower class	35	70.0	29	58.0	[b]0.211[ns]
Middle class	15	30.0	21	42.0	

Table I showed the socio-demographic variables of the study patients, it was observed that more than two third (68.0%) of patients were belonged to age 21-30 years in group I and 39(78.0%) in group II. The mean age was found 28.2±4.5 years in group I and 26.7±4.1 years in group II. Almost three fourth (70.0%) of the patients came from lower-class families in group I and 29(58.0%) in group II. Socioeconomic status and maternal age were not statistically significant ($p<0.05$) between the two groups.

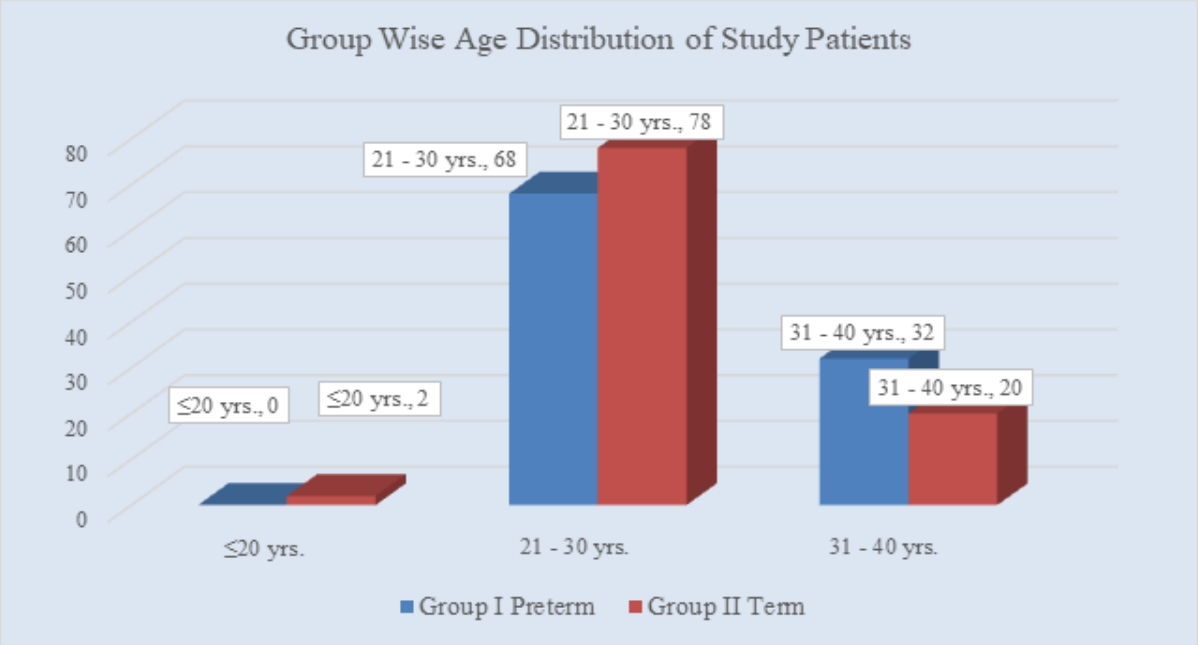

Figure 1: Showed Group Wise Patients Age Distribution (N=100)

Table II: Distribution of the study patients by BMI (N=100)

	Group I (Preterm) (n=50)	Group II (Term) (n=50)	P- value
	Mean ±SD	Mean ±SD	
BMI (kg/m^2)	23.0±3.8	24.4±3.4	0.055^{ns}
Range (min- max)	16.9-31.0	22.0-32.0	

Table 2 showed that the mean BMI was found 23.0±3.8 kg/m^2 in group I and 24.4±3.4 kg/m^2 in group II. The difference was statistically not significant ($p<0.05$) between two groups.

Table III: Distribution of the study patients by obstetrical variable (n=100)

	Group I (Preterm) (n=50)		Group II (Term) (n=50)		P-value
	n	%	n	%	
Parity					
0 (Nulli)	7	14.0	20	40.0	
1 (Primi)	13	26.0	9	18.0	^{a}0.137^{ns}
≥2 (Multi)	30	60.0	21	42.0	
Gravida					
1 (Primi)	7	14.0	20	40.0	^{a}0.003^s
≥2 (Multi)	43	86.0	30	60.0	
Gestational age (weeks)					
Preterm (≤36 weeks)	50	100.0	0	0.0	
Term (37-40 weeks)	0	0.0	50	100.0	
Mean ±SD	33.4 ±2.7		38.9 ±0.8		^{b}0.001^s
Range (min - max)	28-36		38-40		

Table III showed the obstetrical variable of the study patients, it was observed that the majority (60.0%) of patients were ≥2 (multi) para in group I and 21(42.0%) in group II. The majority (86.0%) of patients were ≥2 (multi) gravida in group I and 30(60.0%) in group II. The mean gestational age was found at 33.4±2.7 weeks in group I and 38.9±0.8 weeks in group II. The gravida and gestational age were statistically significant ($p<0.05$) between the two groups.

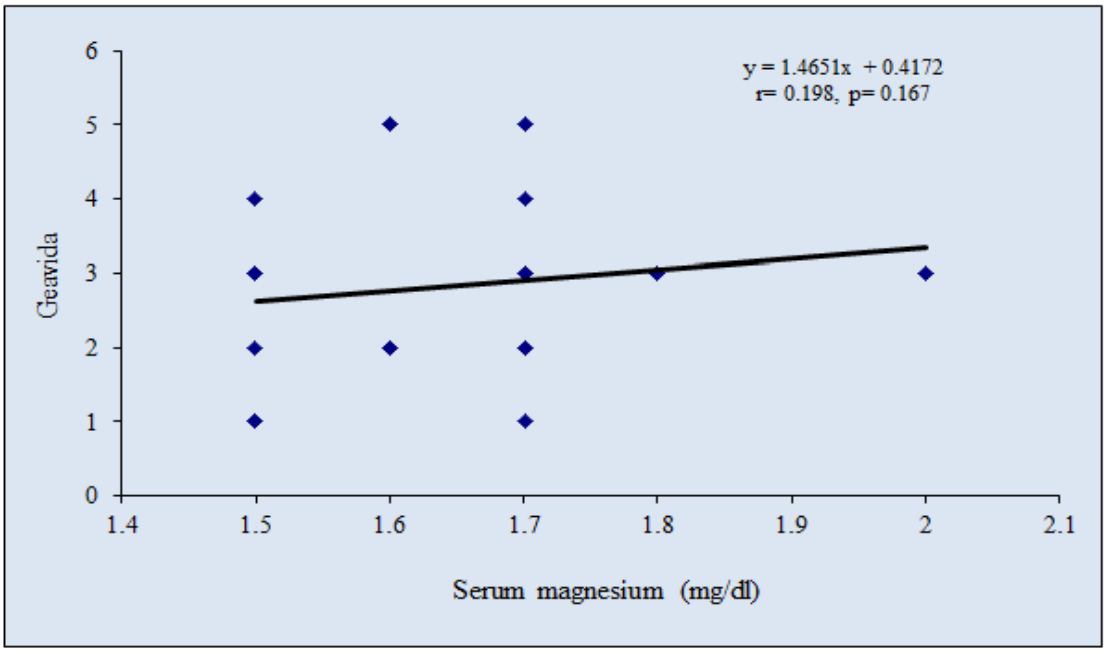

Figure II: Scatter diagram showed positive correlation (r=0.198; p=0.167) between gravida and serum magnesium in group I

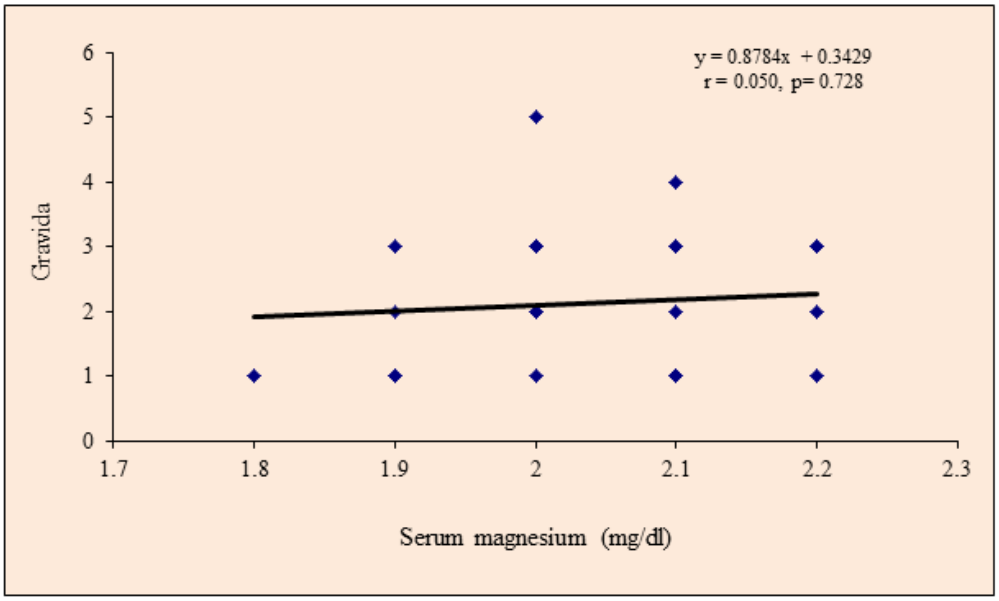

Figure III: Scatter diagram showing no correlation (r=0.050; p=0.728) between gravida and serum magnesium in group II

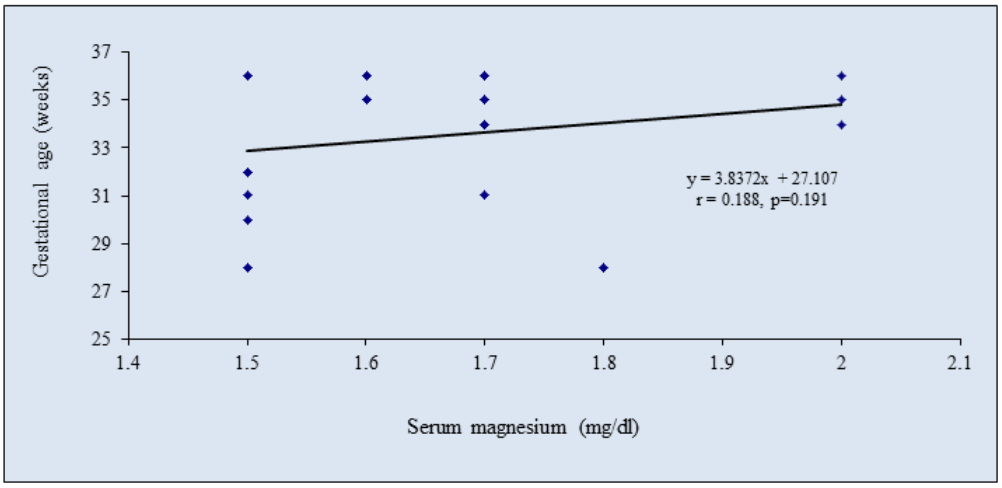

Figure IV: Scatter diagram showing positive correlation (r=0.188; p=0.191) between gestational age and serum magnesium in group I

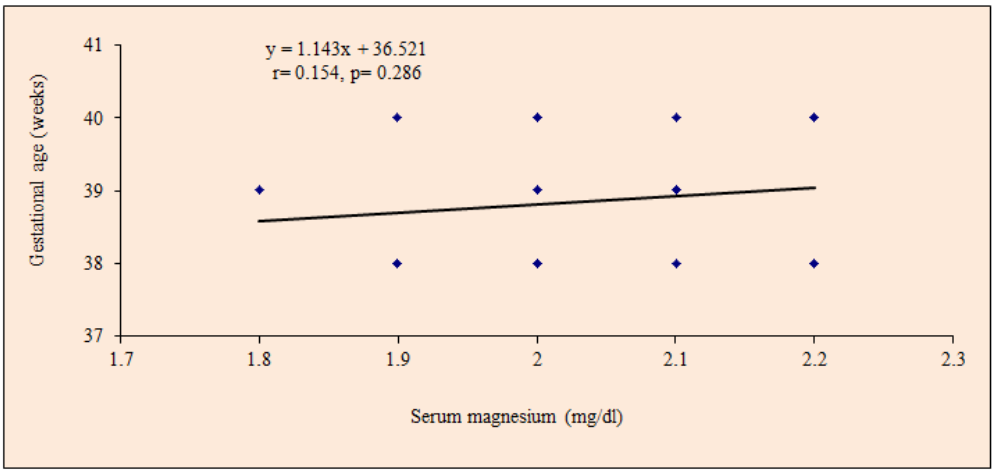

Figure V: Scatter diagram showing positive correlation (r=0.154; p=0.286) between gestational age and serum magnesium in group II

Table IV: Distribution of the study patients by serum magnesium (N=100)

Serum magnesium (mg/dl)	Group I (Preterm) (n=50)		Group II (Term) (n=50)		RR	95% CI	P-value
	n	%	n	%			
<1.8	26	52.0	0	0.0	3.08	2.22 - 4.28	
1.8-2.2 (normal)	24	48.0	50	100.0			
Mean ±SD	1.64 ±0.13		2.05 ±0.11				0.001[s]
Range(min, max)	1.5-2.0		1.8-2.2				

Table IV showed the serum magnesium of the study patients, it was observed that more than half (52.0%) of patients had <1.8 mg/dl serum magnesium level in group I and not found in group II. The mean serum magnesium was found 1.64±0.13 mg/dl in group I and 2.05±0.11 mg/dl in group II. The difference was statistically significant (p<0.05) between the two groups.

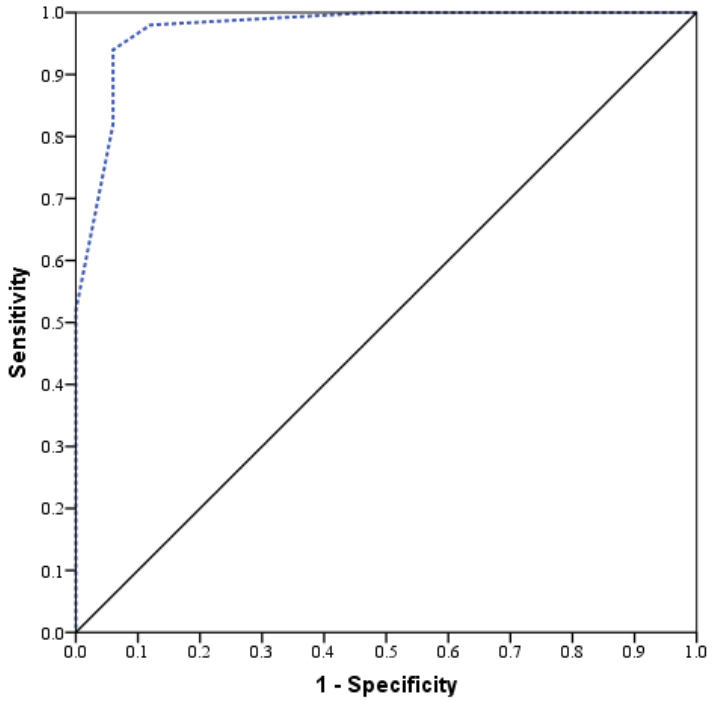

Figure VI: Receiver-operator characteristic curves of serum magnesium level.

Receiver-operator characteristic (ROC) curve of serum magnesium level for prediction of preterm labour

The area under the receiver-operator characteristic (ROC) curves for the prediction of preterm labour is depicted in table VI. Based on the receiver-operator characteristic (ROC) curves serum magnesium had an area under curve 0.974. Receiver-operator characteristic (ROC) was constructed by using serum magnesium, which gave a cut-off value <1.8 mg/dl, with 98.0% sensitivity and 88.0% specificity for the prediction of preterm labour.

Table V: Receiver-operator characteristic (ROC) curve of serum magnesium for prediction of preterm labour

	Cut of value	Sensitivity	Specificity	Area under the ROC curve	95% Confidence interval (CI)	
					Lower bound	Upper bound
Serum magnesium (mg/dl)	<1.8	98.0	88.0	0.974	0.948	1.000

DISCUSSION

The Preterm labour cause is still unknown. In the physiology of parturition, magnesium plays an important role. A decrease of Magnesium in plasma may be responsible for a decrease of the same in myometrium and this might have a considerable influence on the preterm labour. To uterine hyperactivity which leads to cervical dilatation, a Hypomagnesaemia lead to neuromuscular irritability leading [22]. The present study findings were discussed and compared with previously published relevant studies. In this present study, it was observed that more

than two third (68.0%) of patients belonged to age 21-30 years in group I and 39(78.0%) in group II. The mean age was found 28.2±4.5 years varied from 21 – 36 years in group I and 26.7±4.1 years varied from 20 – 35 years in group II. The mean age difference was not statistically significant (p>0.05) between the two groups. In our country, Begum and Das [17] found the mean age was 25.681±5.84 years in preterm and 26.05±5.13 years in the term group which was not statistically significant between the two groups (p>0.50), which is comparable with the current study. In Bangladesh Siddika *et al*., [23] observed the mean (±SD) age of case and control group women were 26.35±4.6 years and 24.26±3.6 years respectively. In Dhaka Medical College Hospital almost similar age ranged also observed by Shahid *et al.*, [19]. Similar observations regarding the mean age were also observed by Okunade *et al*., [13]; Bhat *et al*., [16] and Khani *et al*., [18] In this current study, it was observed that the majority (70.0%) of the patients came from lower-class family in group I and 29(58.0%) in group II. Socioeconomic status was not statistically significant (p<0.05) between the two groups. In our country Siddika *et al*., [23] found that most of their study subjects, both cases and control groups, belonged to middle socioeconomic status (66.7% and 86.7%). In Sri Lanka Bhat *et al*., [16] found the majority (58) patients in preterm belonged to low socio-economic class, whereas in term 45 patients belonged to this class. In this series it was observed that the mean BMI was found 23.0±3.8 kg/m^2 in group I and 24.4±3.4 kg/m^2 in group II. The mean BMI was not statistically significantly (p<0.05) in both groups. Similarly, in our country, Begum and Das [17] found the mean BMI was 23.12±2.36 kg/m^2 in preterm groups and 24.88±1.42 kg/m^2 in the term group, which was also significantly higher term group, which is closely resembled with the present study. In this present study, it was observed a not significant negligible negative correlation (r= -0.125; p=0.368) was found between BMI and serum magnesium in group I. On the other hand, a not significant weak positive correlation (r= 0.219; p=0.127) was found between BMI with serum magnesium in group II. Similarly, in our country, Begum and Das [17] observed the effect of BMI (Body Mass Index) on serum magnesium levels in preterm and term groups. In term group, BMI showed significant difference in serum magnesium level between ≤25 kg/m^2 and >25kg/m^2 groups (p<0.01), while in preterm group, there was no significant difference. In both, the groups mean serum magnesium level was higher in women with BMI >25 kg/m^2 compared to ≤ 25 kg/m^2. In this existing study, it was observed that all (100.0%) patients were found a single number of fetus in utero in group I and group II respectively. The majority (60.0%) of patients were ≥2 (multi) para in group I and 21(42.0%) in group II. Okunade *et al*., [13] showed there was no significant differences between the preterm and term groups distributions regarding the parity, similar findings also observed by Khani *et al*., [18] In this study it was observed that majority (86.0%) of patients were ≥2 (multi) gravida in group I and 30(60.0%) in group II. Multigravida was significantly (p<0.05) more common in group I. Similar observations regarding the gravida was also observed by Broumand *et al*., [24] On the other hand Siddika *et al*., [23] done a study in our country and found 63.3% women of the preterm group and 53.3% of term control group were multipara. In another study in Bangladesh Khan [18] observed multigravida was 58.1% in preterm labour and 44.4%) in term labour. Kansaria *et al*., [25] found 36(65.5%) primigravidas and 19 (34.5%) multigravidas in preterm labour, which are comparable with the current study. In this study it was observed that the mean gestational age was found 33.4±2.7 weeks in group I and 38.9±0.8 weeks in group II. The mean gestational age was significantly (p<0.05) less in group I. In our country Begum and Das [17] found the mean (±SD) gestational age were 33.03±1.83 weeks and 38.95±0.89 weeks in preterm and term group respectively. Similarly, Siddika *et al*., [23] observed the mean (±SD) gestational age of case and control group of women were 34.6±0.97 and 39.23±0.77 weeks respectively. In this present study it was observed that not significant negligible positive correlation (r=0.198; p=0.167) was found between gravida and serum magnesium in group I. But no correlation (r=0.050; p=0.728) was found between gravida and serum magnesium in group II. A not significant negligible positive correlation (r=0.188; p=0.191) was found between gestational age and serum magnesium in group I. There was also a not significant negligible positive correlation (r=0.154; p=0.286) was found between gestational age and serum magnesium in group II. In our country Shahid *et al*., [19] Similar observations regarding the mean age were also observed by Okunade *et al*., [13]; Bhat *et al*., [16] and Khani *et al*., [18] It is known that serum magnesium levels fall during pregnancy with gestational age. This decrease of magnesium plays an important role in the physiology of parturition. In this series it was observed that more than half (52.0%) patients had low (<1.8 mg/dl) serum magnesium level in group I and not found in group II. The relative risk (RR) of the present study indicates that the risk of preterm labour is 3.08 times higher among the patients with low serum magnesium. The mean serum magnesium was found 1.64±0.13 mg/dl varied from 1.5 -2.0 mg/dl in group I and 2.05±0.11 mg/dl varied from 1.8 - 2.2 mg/dl in group II. The mean serum magnesium level was significantly (p<0.05) decreased in group I. Similarly, in Bangladesh Shahid *et al*., [19] found that serum magnesium level to be significantly reduced in the cases of preterm labour. Therefore, their study demonstrated that serum magnesium concentration is decreased in preterm labour. Their study also reported that the patients belonging to lower gestational age have lower serum magnesium level than the patient with higher gestational age. The mean magnesium was found 1.87 ± 0.34 mg/dl for the patients with preterm labour and 2.10

± .04 mg/dl for those with term labour in Shahid *et al*., [19] and the mean magnesium was significantly ($p<0.05$) lower in preterm group. Begum *et al*., [17] also observed that there was a significant reduction ($p<0.05$) and in women with preterm labour of serum magnesium (mean 1.77±0.36). The statistical analysis of Shahid *et al*., [19] study showed that the proportion of low serum magnesium levels is 60.0% among the patients with preterm level compared to normal labour 32.0% that was statistically significant ($p<0.05$). In another study in our country, Begum and Das [17] found the mean serum magnesium level was significantly low in the preterm group of women 1.65±10.19, ranged from 1.30-2.00 mg/dl) compared to term group of women 2.02±0.20, ranged from 1.70-2.40 gm/dl. The above findings are closely resembled with the present study. Okunade *et al*., [13] found 36.0% of their study patients had varying degrees of hypomagnesaemia. It was also exposed that 47.0% of the preterm patients had serum magnesium levels less than 1.6mg/dL, whereas only 25.0% of the term patients had this low serum magnesium level. With low serum magnesium (less than 1.6mg/dL), the relative risk (RR) indicates that the risk of preterm labour is 1.83 times higher among the patients. The mean difference in serum magnesium level in both groups was statistically significant ($p<0.05$). In another study, Bhat *et al*., [16] found the mean serum magnesium level in Group I (preterm group) was found to be 1.343±0.09 mg/dl whereas in Group II (term group) it was 1.875±0.013 mg/dl. The difference between the two groups was found to be statistically highly significant ($p<0.05$). Based on the receiver-operator characteristic (ROC) curves serum magnesium had area under curve 0.974. Receiver-operator characteristic (ROC) was constructed by using serum magnesium, which gave a cut off value <1.8 mg/dl, with 98.0% sensitivity and 88.0% specificity for prediction of preterm labour. Khani *et al*., [18] found the serum magnesium sulfate level was lower than the cutoff point in 19 women in case and 10 in control group as specificity 95.0%, sensitivity 50.0%, positive 66.5% and negative prognostic values 83.33%. On the other hand, Okunade *et al*., [13] found the maternal serum magnesium cutoff value of less than 1.6 mg/dL as a predictive measure of preterm labour using the ROC curve revealed that its sensitivity 50.0%, specificity 52.0%, positive 73.8% and negative prognostic values 60.6%, which differ with the current study.

Limitations of the Study

Although the research has reached its aims, there are limitations that need to be mentioned. The study population was selected from one selected hospital in Dhaka city, so the results of the study may not reflect the exact picture of the country. The present study was conducted in a very short period of time with small sample size which was also a limitation of the present study. Therefore, in future, further studies may be undertaken with large sample size.

RECOMMENDATIONS

Prophylactic oral magnesium supplementation to the patients with a higher risk for the development of preterm labour may be successful for the prevention of preterm labour, as there may be relative deficiency due to increased demand. To decrease the problems related to preterm labor the dietary supplementation of magnesium might deliver an easy and low-cost means. Further studies can be undertaken to find out the aetiology of irritability of the uterus due to low levels of serum magnesium, to evaluate the role of magnesium in preterm labour. As a marker or predictor of idiopathic group of preterm labour, the probability of use of low serum magnesium. A cohort study with the same cut off point and supplementation of magnesium in randomized controlled trial studies is recommended.

CONCLUSION

This study was undertaken to determine the relationship between serum magnesium levels and the onset of preterm labour. This study showed that hypomagnesimia is more profound in preterm labour women and serum magnesium levels showed a significant positive correlation with preterm labour. It may be concluded that the estimation of serum magnesium in pregnancy may prove to be a valuable tool to prevent the preterm onset of labour.

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