

## Risk of Serum Ionized Magnesium among Women with Preeclampsia

### Abstract

**Background:** There are many risk factors of development of preeclampsia among the pregnant women. **Objective:** The purpose of the present study was to measure the risk of serum ionized magnesium level with preeclampsia. **Methodology:** This case-control study was performed in the Department of Obstetrics and Gynaecology, Dhaka Medical College and Hospital from January 2020 to December 2021 for a period of 2(two) years. All pregnant women presented with preeclampsia were The ionized magnesium levels in venous blood drawn from preeclamptic cases. Magnesium levels in pregnant, age-matched, healthy women were also determined. **Result:** A total number of 100 pregnant women included in this study of which 50 pregnant women were designated as case and the rest 50 pregnant women were control. It has found that serum levels of ionized magnesium were significantly decreased among preeclamptic cases ( $0.58 \pm 0.06$ ) as compared to normal pregnancies ( $0.72 \pm 0.05$ ) ( $p < 0.001$ ). Using a cut-off value of 0.7 mmol/l, the serum ionized magnesium level was divided into two groups and was compared between cases and controls. The risk of developing preeclampsia was more than 33 (95% CI = 10.9 – 102.1) times higher in pregnant women with serum magnesium level  $< 0.7$  mmol/L than those pregnant women with serum magnesium level 0.7 or  $> 0.7$  mmol/L. **Conclusion:** Low level of serum ionized magnesium is a risk factor of development of preeclampsia.

**Keywords:** Ionized Magnesium, Preeclampsia, pregnancy, obstetric complications

### Introduction

Pre-eclampsia is a major cause of maternal and fetal mortality and morbidity<sup>1</sup>. This disease is a leading cause of foetal growth restriction, infant morbidity and mortality<sup>1</sup>. The incidence of pre-eclampsia is 2-10%, depending on the population studied and definitions of pre-eclampsia<sup>2</sup>. All over the world preeclampsia is the 3<sup>rd</sup> position for maternal mortality<sup>3</sup>. It also causes maternal death during pregnancy, childbirth and puerperium<sup>4</sup>. In the developing countries, preeclampsia affects 4.4% of all deliveries; however, in Bangladesh the incidence of preeclampsia is very high. It is about 10%-15% of all deliveries<sup>5</sup>.

There are several factors which are responsible for the development of preeclampsia. Interestingly the significant reduction in serum ionized magnesium is found in preeclamptic mother<sup>6</sup>. Generally magnesium has been known as essential cofactor for much enzyme system<sup>7</sup>. The hypomagnesemia in most pregnant women is associated with haemodilution, renal clearance during pregnancy and consumption of minerals by the growing fetus<sup>8</sup>. Serum ionized magnesium level is tightly regulated in a narrow range of approximately 0.7 to 1.1 mmol/L. Serum magnesium level particularly ionized magnesium level is not routinely measured in the developing countries as well as developed countries<sup>9</sup>. Bangladesh is a developing country where higher incidence of preeclampsia was reported. So measurement of serum ionized magnesium level in preeclamptic patient can guide regarding subsequent outcome of the cases and can also help in initiating necessary steps. Therefore this study is designed to know the association of ionized magnesium in preeclamptic women. The purpose of the present study was to evaluate serum ionized magnesium status in preeclampsia.

## **Methodology**

This case-control study was conducted in the Department of Obstetrics and Gynaecology at Dhaka Medical College and Hospital, Dhaka from January 2020 to December 2021 for a period of two (02) years. It was taken from IPD and OPD of Obstetrics and Gynaecology Department of DMCH. Pregnant women with gestational age between 24 and 40 weeks with features of preeclampsia having >90 mmHg diastolic blood pressure and >140 mmHg systolic BP with proteinuria 1+ or more by Dipstick test of two random clean catch urine specimen collected at least 4 hrs apart after exclusion of other urinary pathology were taken as case and pregnant women of gestational age between 24 and 40 weeks without preeclampsia within normal range of systolic and diastolic blood pressure and free from any medical or obstetric complications were taken as control. Purposive sample method was followed as per inclusion and exclusion criteria. Evaluation of the patient was based on history, physical examination and investigations. Patient with known acute or chronic renal disease, diabetes mellitus, heart failure, hepatic dysfunction or known case of thyroid dysfunction were excluded from this study. All cases and controls were given an explanation of the study and informed consent was taken. Data was collected using the structured

designed by interview, observation, clinical examination, biochemical investigation from history sheet of the patient. Under aseptic precaution 2 cc venous blood was taken with disposable plastic syringe from the antecubital vein and then blood was transferred to a test tube for determination of serum ionized magnesium. The investigation was done by the department of Biochemistry BIRDEM Hospital. Multi system automatic analyzer was used as analyzer instrument. Using a cut-off value of 0.7 mmol/l, the serum ionized magnesium level was divided into two groups and were compared between cases and controls to see the association of serum ionized magnesium with preeclampsia as well as to estimate the risk of developing preeclampsia in women with low serum ionized magnesium. Data were processed and analyzed using computer based SPSS (Statistical Package for Social Sciences) version 11.5. The test statistics used to analyse the data were descriptive statistics, Chi-square ( $\chi^2$ ) test, Students t test and Odds Ratio. For all analytical tests the level of significance was 0.05 and  $p < 0.05$  was considered significant.

## Results

A total of 100 pregnant women were taken as study populations of which 50 pregnant women with preeclampsia were in case group and the rest 50 were in control. Nearly half (48%) of the patients in group A was 25 or below 25 years followed by 26 – 30 years (34%) and more than 30 years of age (18%). In control group, majorities were  $\leq 25$  years (46%) followed by 26-30 years (38%) and more than 30 years of age (16%). The mean age was almost identical between case ( $26.6 \pm 5.7$ ) and control ( $26.2 \pm 5.3$ ) ( $p=0.909$ ) (Table I). Sixty percent of the patients in cases had gestational age 34 or below 34 weeks and the remaining 40% above 34 weeks, while in control 58% of patients had gestational age 34 weeks or below and 42% more than 34 weeks ( $p = 0.839$ ). Primi-gravida was observed to be higher in case (56%) than control (40%) ( $p=0.109$ ). Past PET was significantly higher in case (14%) than in control (2%) ( $p<0.05$ ). The mean systolic ( $160.2 \pm 15.5$ ) and diastolic ( $103.6 \pm 22.1$ ) BP was significantly higher in cases ( $106.2 \pm 18.3$ ) compared to control ( $67.8 \pm 8.9$ ) ( $p<0.001$ ) (Table II). Low serum ionized magnesium ( $<0.7$  mmol/L) was observed to be significantly associated with cases than that of their control counterpart (88% vs. 18%,  $p<0.001$ ). The risk of developing preeclampsia was more than 33 (95% CI 10.9-102.1) times higher in pregnant women with serum ionized magnesium  $< 0.7$  mmol/L than those pregnant women with serum ionized magnesium 0.7 or  $> 0.7$  mmol/L. (Table III)

**Table I: Age distribution between groups (n = 100)**

Age (years)	Group		p-value
	Group-A (n = 50)	Group-B (n = 50)	
≤ 25	24(48.0)	23(46.0)	0.909
26 - 30	17(34.0)	19(38.0)	
> 30	9(18.0)	8(16.0)	
<b>Mean ± SD</b>	<b>26.6 ± 5.7</b>	<b>26.2 ± 5.3</b>	

Figures in the parentheses indicate corresponding percentage; Student's t-Test was done to analyse the data;

**Table II: Distribution of patients by gestational age between groups (n = 100)**

Different Variables	Group		p-value
	Case (n = 50)	Control (n = 50)	
Gestational age (weeks) ≤ 34	30(60.0)	29(58.0)	0.839
Gravida (Primi)	28(56.0)	20(40.0)	0.109
Past history of PET	7(14.0)	1(2.0)	0.030
Systolic BP	160.2 ± 15.5	103.6 ± 22.1	<0.001
Diastolic BP	106.2 ± 18.3	67.8 ± 8.9	<0.001

Figures in the parentheses indicate corresponding percentage; # Chi-square ( $\chi^2$ ) Test was done to analyse the data; Student's t-Test was done to analyse the data and data are presented as mean ± SD.

**Table III: Comparison of serum ionized magnesium between Case and Control**

S ionized magnesium (mmol/L)	Group		p-value <sup>#</sup>	OR(95% CI)
	Case (n = 50)	Control (n = 50)		
< 0.7	44(88.0)	9(18.0)	< 0.001	33.9 (10.9-102.1)
≥ 0.7	6(12.0)	41(82.0)		
<b>Mean ± SD</b>	<b>0.58 ± 0.06</b>	<b>0.72 ± 0.05</b>		

Data were analyzed using  $\chi^2$  Test; figures in the parentheses denote corresponding %; Odds Ratio estimates the risk of developing an event in the case group compared to the control group.

## Discussion

Preeclampsia is one of the most important obstetric complications leading to significant maternal and foetal mortality and morbidity<sup>4</sup>. Several medical investigations have suggested that magnesium (Mg) deficiency could play an important role in the pathogenesis of preeclampsia, particularly in regulating the tonus of arterioles and veins<sup>6,10-13</sup>. A total number of 100 pregnant women were included in this study in whom the numbers of preeclamptic cases were 50 and controls were 50. The mean age was almost identical between groups ( $p=0.730$ ). Several studies conducted in this regards<sup>14-15</sup> have shown similar age distribution between preeclamptic women and normal pregnancies. Standley *et al* (1997) have reported relatively younger age subjects in both controls and cases. Sixty percent of the patients in Cases had gestational age 34 or below 34 weeks and the remaining 40% above 34 weeks, while in Control 58% of patients had gestational age 34 weeks or below and 42% more than 34 weeks. Primi gravida was observed to be higher in Case (56%) than that in Control (40%). Incidence of past PET was higher in Case than that in control. However, the obstetric variables like gestational age, gravida were all homogeneously distributed between groups. The mean systolic blood pressure ( $p < 0.001$ ) and mean diastolic BP was significantly higher in cases compared to control ( $p < 0.001$ ). Sukonpan and Phupong<sup>14</sup> demonstrated that systolic blood pressure and diastolic blood pressure are higher in the preeclamptic group than that of normal pregnancies which is consistent with our present study.

In this study, low serum ionized magnesium ( $< 0.7$  mmol/L) was observed to be significantly associated with cases than that of their control counterpart. Forty four (44) women with preeclampsia (Case) had serum magnesium level  $< 0.7$  mmol/L whereas only 9 pregnant women from the Control group had this level of serum magnesium (88% vs. 18%,  $p < 0.001$ ). Comparison of serum ionized magnesium level between mild and severe preeclampsia showed that severe preeclampsia had significantly lower mean magnesium level ( $0.56 \pm 0.04$  mmol/L) than that in mild preeclampsia ( $0.63 \pm 0.05$  mmol/L) ( $p < 0.001$ ). Sukonpan and Phupong<sup>14</sup> had done a study where they included 40 preeclamptic cases and 40 normal pregnant women as control. The mean serum ionised magnesium concentrations in those normal pregnant women ( $0.85 \pm 0.09$  mmol/l) was within the range (0.65- 1.11 mmol/l) given by previous reports<sup>16-18</sup>. On the other hand, the mean serum ionised magnesium levels in preeclamptic group of their study was significantly lower ( $0.77 \pm 0.08$  mmol/l,  $p= 0.001$ ) than that of normal pregnant ladies. They have tried to make a comment that hypomagnesemia in most pregnant women is associated with haemodilution, renal clearance during pregnancy and consumption of minerals by the growing fetus<sup>14</sup>. Handwerker *et al*<sup>16</sup> performed a research

work including 12 preeclamptic woman as case and 33 normal pregnant ladies as control where estimations of serum ionized magnesium was carried out in both groups. It was apparent that mean level of serum ionised magnesium were significantly decreased in preeclamptic patients than that of normal pregnancies. The results and outcome of our present study was quiet similar to other research works done in the past. In this study association between hypomagnesemia and preeclampsia had been clearly noted. The odds ratio had shown that the risk of developing preeclampsia was more than 33 (95% CI = 10.9 – 102.1) times higher in pregnant women with serum ionized magnesium level < 0.7 mmol/L than those pregnant women with serum magnesium level 0.7 or > 0.7 mmol/L. Here the p-value is < 0.001 which is statistically significant. Like most scientific studies, the present study was not within limitations. One methodological limitations of the study was, use of purposive sampling procedure. The findings of the study must be interpreted with caution, particularly in case of generalization. Dietary intake of magnesium by each participant may vary which may also affect the results of the study. Undiagnosed chronic hypertension or renal disease may be mistaken as features of preeclampsia. Disturbances in the serum level of other cations were not measured in this study which may have pathophysiological effects on the occurrence of preeclampsia.

## **Conclusion**

In conclusion, significant differences of serum ionized magnesium levels is detected in preeclamptic patients as compared to healthy pregnant women. Further investigations of disturbances of intracellular and extracellular magnesium and other cations metabolism in preeclampsia should be carried out.

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