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Original Research Article

## Serum magnesium at 18-20 weeks of gestation: can it be a predictor of gestational hypertension and fetomaternal outcome?

Sasikala Kathiresan<sup>1</sup>, Agalya Angelina Sanjevrajah<sup>1\*</sup>, Jeyashree Kathiresan<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, <sup>2</sup>Department of Preventive and Social Medicine, Velammal Medical College Hospital and Research Institute, Anuppanadi, Madurai, Tamil Nadu, India

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### \*Correspondence:

Dr. Agalya Angelina Sanjevrajah,  
E-mail: [cmcmdr.angelina@gmail.com](mailto:cmcmdr.angelina@gmail.com)

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### ABSTRACT

**Background:** Hypertensive disorders of pregnancy (HDP) is a major cause of maternal, fetal morbidity and mortality complicating 10% of all gestations. As effective treatments are very limited, prediction of HDP occurrence is most importance. Though many biomarkers have shown relationship with HDP, serum magnesium (Mg) has shown better predictor as involved in maintaining vascular contractility, tone. This study is intended to analyse incidence of GHT and fetomaternal outcome in pregnant women with normal and low serum magnesium level measured at mid trimester (18-20 weeks).

**Methods:** A total of 105 consecutive singleton pregnant women in between 18-20 weeks of gestation attending OBG outpatient department were enrolled. After obtaining the informed consent, structured proforma was used to collect demographic, clinical details. Serum magnesium was measured by the colorimetric method and study participants were divided into two groups based on Mg cut off 1.5 mg/dl and followed up throughout pregnancy for fetomaternal outcome.

**Results:** This study results revealed that 35.2% (37/105) pregnant women had serum Mg level < 1.5 mg/dl and mean value of Mg of all participant is 1.7 mg/dl, just above the lower limit. During follow-up of these two groups, statistically significant correlation between serum Mg levels (< 1.5 mg/dl) with GHT (8/12) occurrence and pre term birth was found. Other fetomaternal outcome not had significant correlation.

**Conclusions:** As per the findings, serum Mg concentration measurement in between 18-20 weeks can be considered as a one of the predictors for subsequent occurrence of maternal outcome of GHT and fetal outcome of pre-term birth.

**Keywords:** Fetomaternal outcome, Gestational hypertension, Predictor, Serum magnesium

### INTRODUCTION

Hypertensive disorders of pregnancy (HDP) such as gestational hypertension (GHT), pre-eclampsia (PE) are the frequently encountered complications during pregnancy, complicating up to 10% of gestations.<sup>1,2</sup> Globally HDP remains one of the most common cause of maternal, fetal morbidity and mortality.<sup>3,4</sup> Prevalence of GHT and PE in developing countries is 3-10% and 4-18% respectively.<sup>5-7</sup> Women with HDP is associated with increased risks of placental abruption, cerebrovascular

events, disseminated intravascular coagulation and leading to 10-15% of maternal death.<sup>4,8</sup>

Fetus of these mothers are having the increased risk of prematurity, intrauterine growth retardation and death.<sup>9,10</sup> The prevalence of maternal, fetal complications associated with HDP vary by region and healthcare facility type.<sup>11,12</sup> Rate of HDP is likely to increase along with obesity and metabolic syndrome in women of reproductive age group. As effective treatments are

currently limited for HDP, prediction of HDP occurrence is at most importance to prevent the complications.<sup>8,13</sup>

Combination of maternal demographic characteristics, medical and obstetric history, uterine artery pulsatility index, mean arterial pressure and maternal serum pregnancy-associated plasma protein-A and placental growth factor at 11-13 weeks gestation are all used as predictor of HDP.<sup>14-16</sup> Also results from various studies have shown the relationship between hypertensive disorders of pregnancy and serum electrolytes particularly calcium and magnesium.<sup>17,18</sup>

Magnesium is an important cofactor in a number of biochemical reactions in synthesis of proteins, nucleic acids and metabolism of carbohydrates and also in balancing oxidative stress. Apart from that, Mg is important for the normal muscular functions, regulation of potassium, calcium and sodium transport across membranes, maintain vascular contractility and tone. The deficit of Mg is accompanied with the increased risk of endothelial dysfunction and hypertension.<sup>19</sup> The recommended Mg amount on a daily basis increases by 30% during pregnancy and in developing countries as many as 45% of pregnant women are Mg-deficient.<sup>20</sup>

Many studies that have looked into Mg serum concentration in pregnant women with the diagnosis of preeclampsia, but very few studies measured the magnesium level as a base line since the beginning of their pregnancy.<sup>11,12,15,18</sup> And also role of magnesium deficiency in the development of adverse outcomes in terms of both maternal and fetal health was insufficiently studied in the environment.

So, this study is intended to analyse the incidence of GHT and fetomaternal outcome in pregnant women with normal and low serum magnesium level measured at mid trimester (18-20 weeks).

## METHODS

This prospective study was carried out in the department obstetrics and gynecology of this tertiary care centre, spanned over a period of 6 months (October 2017 to March 2018) after attaining the Institutional Ethics Committee approval (IEC Ref No.: VMCIEC/55/2017).

After getting the written informed consent 105 consecutive singleton pregnant women in between 18-20 weeks of gestation attending outpatient department of OBG were enrolled in the study. Pregnant woman with chronic hypertension, pre-existing diabetes, proteinuria, renal diseases and those not willing for participation were excluded from the study. Structured proforma was used to collect demographic and clinical details like age, parity, gestational age of pregnancy based on last menstrual period or ultra sound data and previous existing illness. Blood pressure and urine protein were monitored as a routine to rule out HDP. New-onset

hypertension (systolic blood pressure (SBP)  $\geq$  140 mmHg or diastolic blood pressure (DBP)  $\geq$  90 mmHg on at least two occasions with an interval of 6 hours or more) and proteinuria (urinary excretion of  $\geq$  300 mg of proteins within 24 hours) after 20 weeks of gestation was labelled as PE, and only elevated BP without proteinuria was labelled as GHT.<sup>8</sup>

Five milliliters of venous blood sample was collected in red vacutainer from participant's antecubital vein and immediately transferred to department of Biochemistry where blood samples were allowed to clot at room temperature and then centrifuged at 1500 rpm for 15 minutes for serum separation. Serum magnesium was measured by the colorimetric method using Xylidyl blue with ATCS auto-analyser. Based on the serum Mg level study participants were divided into 2 groups. One with the serum Mg level of  $<$  1.5 mg/dl and another one as serum Mg level of  $\geq$  1.5 mg/dl.

Subsequently all the participants were followed-up till delivery and data recording mode of delivery, development of GHT/PE, maternal and fetal outcomes/complications were documented in the same structured proforma.

## Statistical analysis

The data were analyzed using the SPSS software version 15.0 and expressed in terms of mean, standard deviation, and percentage. Continuous variables were compared with the Student's t-test and paired sample t-test. A p value of  $<$  0.05 was considered as statistically significant.

## RESULTS

A total of 105 singleton pregnant women were included in this study. All of them were in the age group of 18-37 years (mean age $\pm$ SD = 24.8 $\pm$ 3.6), with the gestation period between 18-20 weeks (mean $\pm$ SD = 19.2 $\pm$ 0.7). Half of the participants were primi gravida and another half were multi gravida. Mean serum Mg level among participants were 1.71 $\pm$ 0.55 mg/dl (Table 1).

**Table 1: Demographic and clinical characteristics of the participants.**

	Mean/N	SD/%
Age (years)	24.86	3.56
<b>Gravida</b>		
Primi	52	49.5
Multi	53	51.5
Serum Mg (mg/dl)	1.71	0.55

This study participants were divided into 2 groups based on the serum Mg level cut off of 1.5 mg/dl. Among the 105 participants, 37 pregnant women (35.2%) had the serum Mg level below 1.5 mg/dl were categorised as Group I and 68 pregnant women (64.8%) had the serum

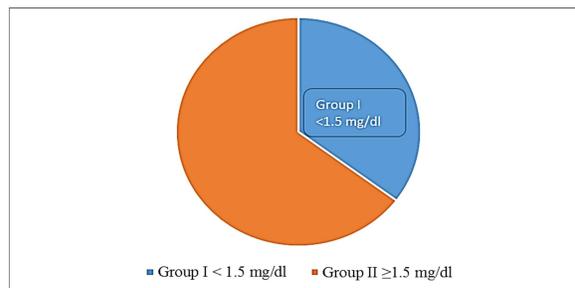
Mg level  $\geq 1.5$  mg/dl were categorised as Group II (Figure 1).

During the next visit, total of 12 pregnant women (8 pregnant women from Group I and 4 from Group II) has developed the GHT. Analysing GHT development among both the groups revealed that there were statistically significant correlation between serum Mg levels of less than 1.5 mg/dl with GHT occurrence with the p value of 0.015 ( $p < 0.05$ ) (Table 2).

In Group I among 37 pregnant women who had serum Mg level  $< 1.5$  mg/dl, 9 pregnant women had urinary albumin positive, 2 developed gestational diabetes, 6 had oligohydramnios and 2 had meconium stained liquor. Analysing fetal complications 3 had IUGR and another 3 had preterm babies.

In Group II among 68 pregnant women who had serum Mg level  $\geq 1.5$  mg/dl, 10 pregnant women had urinary albumin positive, 9 pregnant women developed gestational diabetes, 8 had oligohydramnios and 3 had

meconium stained liquor. Analysing fetal complications 3 had IUGR and another 2 had preterm babies.



**Figure 1: Participant group based on serum magnesium cut off 1.5 mg/dl.**

Analysing correlation between serum Mg level with fetomaternal complications revealed that there were no statistically significant correlation found between these two groups except with preterm birth (Table 3).

**Table 2: Correlation of serum Mg level with GHT occurrence.**

		Group I serum Mg $< 1.5$ mg/dl		Group II serum Mg $\geq 1.5$ mg/dl		Chisq/t	p value
		Mean/N	Sd/%	Mean/N	Sd/%		
GHT	No	29	31.2	64	68.8	5.864	0.015
	Yes	8	66.7	4	33.3		

**Table 3: Correlation of serum Mg level with fetomaternal complication.**

		Group I serum Mg $< 1.5$ mg/dl		Group II serum Mg $\geq 1.5$ mg/dl		Chisq/t	p value
		Mean/N	SD/%	Mean/N	SD/%		
Urine Alb	No	28	32.6	58	67.4	1.496	0.221
	Yes	9	47.4	10	52.6		
GDM	No	35	37.2	59	62.8	1.566	0.211
	Yes	2	18.2	9	81.8		
Oligo hydr	No	31	34.1	60	65.9	0.411	0.522
	Yes	6	42.9	8	57.1		
MSL	No	35	35	65	65	0.052	0.819
	Yes	2	40	3	60		
IUGR	No	34	34.3	65	65.7	0.608	0.436
	Yes	3	50	3	50		
Preterm	No	27	34	66	66	6.432	0.012
	Yes	10	60	2	40		

\*\*\*Alb: Albumin, Oligo hydr: Oligo hydramnios, MSL: Meconium stained liquor, IUGR: Intra uterine growth retardation.

## DISCUSSION

Studies carried out on animal revealed that hypomagnesemia had marked effects on processes of parturition, postpartum uterine involution, fetal growth and development.<sup>21,22</sup> Serum optimum concentration of Magnesium depends on an adequate intake, absorption

and excretion along with availability of Mg from bones. Recommended amount of Mg intake on daily basis is 310-320 mg/day.<sup>19</sup> As pregnancy is associated with hemodilution, increased renal clearance and demand by growing foetus, recommended Mg amount increases 30% on daily basis during the pregnancy. Literature also suggests that over 50% of reproductive age group do not

take the recommended amount of Mg.<sup>11,18</sup> The role that Mg in PE pathogenesis has not been completely elucidated yet. Though contradicting results obtained from different studies, due to its vasodilatory properties Mg can improve the endothelial function and can reduce placental ischemia, which in turn reduce the prevalence of PE.<sup>19</sup>

Mostly evaluation of serum Mg concentration was done in cases where pregnant women had already been diagnosed with PE. In pregnancy determination of serum Mg level is rarely done as a routine clinical protocols though some studies claim that hypomagnesemia is present in as many as ~ 45% pregnant women in certain regions.<sup>12,23</sup> So this study has planned to determine serum concentration of Mg in pregnant women attending this OPD in between 18-20 weeks gestation (i.e., before development of PE which usually occur after 20 weeks).

This study results revealed that 35.2% (37/105) pregnant women enrolled in this study had serum Mg level < 1.5 mg/dl which was concordance with the study finding of Pathak et al, who also reported that 43.6% of pregnant women in India had hypomagnesemia.<sup>24</sup> Also, this study population mean value of serum Mg is 1.7 mg/dl, just above the lower limit. This may be attributed to increased metabolic demand due to growing foetus along with poor nutrition in this setup.

During the follow-up of these two groups, 12 pregnant women (11.4%) developed GHT. Of which two third cases (8/12) from Group I (serum Mg level < 1.5 mg/dl). In comparing both the groups, 21.6% (8/37) of pregnant women developed GHT in Group I; on the other hand, 0.06% (4/64) of pregnant women only developed GHT in Group II. Analyzing GHT development among both the groups revealed that there were statistically significant correlation between serum Mg levels of less than 1.5 mg/dl with GHT occurrence with the p value of 0.015 ( $p < 0.05$ ). This study finding revealed that low serum Mg level during the 18-20 weeks of gestation can be used as one of the predictors of GHT occurrence.

Analyzing the other maternal outcome among these two groups revealed that there were no statistically significant correlation found between serum Mg level and other maternal outcome like gestational diabetes, oligohydramnios and meconium stained liquor. But analyzing the fetal outcome revealed that preterm birth occurrence had the statistically significant correlation with the serum Mg levels of less than 1.5 mg/dl with the p value of 0.012 ( $p < 0.05$ ) as nearly one third of the pregnant women (10/37) in Group I had the preterm birth. This study results are in concordance with Shahid et al, and Enaruna et al, who also reported the same.<sup>12,25</sup> This may attribute due to action of magnesium in pre-term labor attenuation by competing with intracellular calcium at its binding sites, thereby decreasing muscle contractility and stabilizing the membrane potential. This study finding revealed that low serum Mg level during

the 18-20 weeks of gestation can be used as one of the predictors of preterm birth babies.

On analyzing IUGR with serum Mg level revealed that there was no statistically significant correlation in between these two. This may be due to the symphysiofundal height measurement what we have used. Ultrasound diagnosis of IUGR may be a better parameter to analyze with respect to magnesium deficiency.

## CONCLUSION

According to the results obtained from this study, serum Mg concentration measurement in between 18-20 weeks can be considered as a one of the predictors for subsequent occurrence of maternal outcome of GHT. This study results were consistent with the hypothesis that Mg deficiency can account for etiopathogenesis of PE. Besides, serum Mg concentration could also play an important role in predicting the fetal outcome of preterm baby. Taking this into account, determination of serum Mg concentration should be included as a routine practice before occurrence of HDP (before 20 weeks).

## Implication

Predicting the HDP is at most importance to prevent the maternal, fetal complications associated with HDP. As this study results shown serum Mg concentration in between 18-20 weeks of gestation can be used as a predictor of HDP. This will be helpful in taking the preventive measures like nutritional counselling to maintain the positive Mg balance and improving the socio-economic status through education and Mg supplementation or consumption of a Mg-rich diet to all pregnant woman in this study setup to prevent the fetomaternal outcome of HDP.

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