RESEARCH

THE ROLE OF SERUM MAGNESIUM IN PREGNANCY INDUCED HYPERTENSION

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Abstract: Pregnancy induced hypertension or preeclampsia is triad of hypertension, proteinuria and edema occurring after 20 weeks of gestation in previously normotensive women. The aim of the study is to analyze and compare the concentration of serum Magnesium level in women with preeclampsia and in normal pregnant women. **Material and Methods:** This is a cross sectional case-control study involving 25 women with pre-eclampsia in case group and 25 normal pregnant women in control group. The inclusion criteria for case group were age group in between 20-40 yrs including both primi and second gravida in third trimester of pregnancy (>24 weeks of pregnancy). The blood pressure measured by sphygmomanometer in upper arm in sitting posture was ≥140/90mmHg in two different occasions taken 6 hours apart. The urine albumin was ≥1+ or in the mid stream random sample of urine. The controls group was formed by 25 age matched normal pregnant women either primi or second gravida in third trimester of pregnancy. The patients with medical complications such as Diabetes Mellitus, renal failure, chronic hypertension, heart failure or ischaemic heart disease, multiple pregnancies, pregnancy < 24 weeks of gestation, patients on magnesium sulphate and calcium lactate therapy were excluded from the study. The Body Mass Index (BMI), serum calcium and zinc levels were compared between the case and control groups. **Results:** The BMI was significantly higher in preeclamptic women when compared to normal pregnant women 28.71±4.70 versus 22.46±3.42 P<0.001. The serum Magnesium levels in preeclamptic women were significantly lower when compared to normal pregnant women 1.62 ± 0.16 versus 1.92 ± 0.16 P< 0.001 for cases and controls respectively. **Conclusion:** Although the serum Magnesium deficiency cannot be pinpointed as the sole factors for the etiology of preeclampsia, they have a definite role in the development of preeclampsia.

INTRODUCTION

Nutritional deficiencies are common during pregnancy. Pregnant women in the developing countries have been reported to consume diets that are low in minerals and vitamins. An inadequate dietary intake before and during pregnancy might be a risk not only for the mother but also for the fetus. Deficiency of the elements such as magnesium, zinc have been implicated in the pregnancy wastage, congenital anomalies, pregnancy induced hypertension, placental abruption of membrane, low birth weight and still births[1-5].

Magnesium has been known as the essential cofactor for many enzyme systems. It plays an important role in neurochemical transmission and peripheral vasodilatation[6-8].

Pregnancy induced hypertension or preeclampsia is a transient but potentially dangerous complication of pregnancy, with worldwide significance to the mother and the infants. It affects approximately 5-10% of the pregnancies worldwide and results in 15% of preterm deliveries and 14% of maternal deaths per year[9-11]. In the developing countries, preeclampsia accounts for 20-80% of the strikingly increased maternal mortality. In India the incidence of preeclampsia is reported to be 8-10% of pregnancies[12-15].

Preeclampsia has been dubbed as the 'Disease of theories' because of the multiple hypothesis that have been proposed to explain its occurrence[16]. Although many pathophysiologic factors such as inflammation, cytokine production, dyslipidemia[17], elevated homocysteine[18], oxidative stress[19], reduced calcium intake and excretion and an imbalance between the thromboxane and prostacyclin[20],have been implicated in the etiology of preeclampsia, the complete etiologies have not been fully elucidated[12].

Although the high rate of preeclampsia in developing countries has forced some authors to propose the involvement of the nutrition, especially the trace elements in the etiology of the disorder[7], studies on the relationship between the maternal serum trace elements concentrations and the preeclampsia have produced inconsistent results[13].

Hence this study is taken up to analyze and to compare the concentrations of Magnesium in the serum of women with preeclampsia and in the normal pregnant women and to evaluate their role in the pregnancy induced hypertension.

It is hoped that this study will contribute to the knowledge of the role of serum Magnesium in pregnancy induced hypertension.

AIMS AND OBJECTIVES:

This study involves

The estimation of serum Magnesium levels in preeclamptic women in their third trimester of

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pregnancy as case group.

The estimation of the serum Magnesium levels in age matched healthy normotensive pregnant women in third trimester as control group.

Comparison of concentration of Magnesiumin the serum between the case and the control group.

To evaluate the role of Magnesium in pregnancy induced hypertension.

MATERIAL and METHODS

This is a cross sectional case - control study conducted in the Department of Obstetrics & Gynecology, Government Rajaji Hospital, Madurai during the period from 20/6/2011 to 20/8/2011.

The Ethical and Research committee of Madurai Medical College and Hospital approved the study protocol.

Participants:

The study was conducted in 50 pregnant women of age group between 20 – 40 years. Of them, case group comprised of 25 pregnant women either primi or second gravida in third trimester (> 24 weeks of pregnancy) with preeclampsia admitted as in patients in Department of Obstetrics and Gynecology.

The diagnosis of preeclampsia was based on clinical criteria with blood pressure≥ 140/90mmHg measured on two occasions 6 hours apart with proteinuria ≥1+ dipstick along with edema (NHBPEP Classification).

The control group was formed by 25 normal pregnant women either primi or second gravida in third trimester > 24 weeks of pregnancy receiving antenatal care as out patients.

Exclusion criteria used for selecting participants:

Medical complicating pregnancy such as Diabetes Mellitus, Renal failure, Chronic hypertension, Heart failure, Multiple pregnancies and Pregnancy ≤ 24 weeks of gestation. Patients on magnesium sulphate and calcium lactate therapy were excluded from study.

Examination of pedal edema:

A firm pressure was applied over the medial malleolus on both legs for 15 seconds in all participants and looked for pitting in that region to confirm the presence of pedal edema.

Anthropometry:

The heights of the participants were measured using standard methodology with the help of non-stretchable inch tape. The weights of the participants were measured using a weighing machine and BMI was calculated using Quetlet Index using the formula Wt (kg)/ht (mt) 2.

Measurement of Blood pressure:

With a standard sphygmomanometer and stethoscope the systolic and diastolic blood pressure of all participants were measured in the right upper arm in sitting posture by Auscultatorymethod. The first and fifth Korotkoff's phase were recorded as systolic and diastolic blood pressure respectively. The blood pressure for cases group was recorded at two occasions one at 9.00 am and another at 5.00 pm using the same procedure.

Estimation of urine albumin:

Clean catch midstream random urine sample was obtained from all participants. The urine protein was measured by dipstick method using Dip N Read reagent strip. The results was graded on the scale of 0 to 4+ (0, none; 1+, 30 mg/dl; 2+, 100 mg/dl; 3+, 300 – 1,999 mg/dl; 4+ ≥ 2000 mg/dl).

Blood sample collection:

Three ml of blood was drawn in all the participants from the cubital vein by using dispovan. The blood drawn was collected in a vaccum tube.

Serum separation:

The blood samples were allowed to clot spontaneously at the room temperature. Then the clotted blood was centrifuged at 3,000rpm for 10 minutes. The serum separated was stored at 2 - 8 degrees Celsius until analysis.

Estimation of Serum Magnesium:

Method: Calmagite method.

Principle:

Magnesium combines with calmagite in an alkaline medium to form a red colour complex. Interference of calcium and proteins are eliminated by adding specific chelating agents and detergents. Intensity of the colour formed is directly proportional to the amount of magnesium present in the sample.

Magnesium + calmagite → Red coloured complex

Reagents:

R 1	Calmagite	0.14 mM/L
	Potasium Chloride	77 mM/L
	Polyvinylpyrrolidine	0.03 mM/L
R2	Potasium cyanide	1.5 mM/L
	Potassium Hydroxide	14.3 mM/L
S	Magnesium standard	2.0 mEq/L

Working reagent: Working reagent was prepared by mixing the equal volume of R 1 and R 2.

Stability: The working reagent is stable at 2 - 80 C for one month.

Procedure:

Pipette into vials	Blank **(B) ml**	**Standard (S) ml**	**Test (T) ml**
Serum			0.01
Magnesium standard		0.01 ml	
Working Reagent	1 ml		
Distilled water	0.01 ml		

The reagents were pipetted into clean dry test tube. Mixed well and incubated at room temperature (250 C) for 5 minutes. The absorbance was measured in analyzer at 510 nm first with standard against blank sample and then for the test sample against blank sample.

Calculation:

$$\text{Magnesium in mmol/L} = \frac{\text{Absorbance of test}}{\text{Absorbance of standard}} \times 2$$

Conversion factor: Magnesium concentration mg/dl = Mg concentration mmol/L X 2.43

RESULTS

Contents	**Cases (n=25) (mean±SD)**	**Controls (n=25) (mean±SD)**	**p-value**
Age (yrs)	23.80±3.48	23.52±2.52	0.746
BMI (kg/m^2)	28.71±4.70	22.46±3.42	<0.001
Gravida	1.480 ±0.51	1.52± 0.510	0.783
Parity	0.48 ±0.510	0.520 ±0.510	0.783
Weeks of gestation (Wks)	32.56±4.34	32.56±3.48	1.000
Pulse (/min)	97.36±8.56	94.16±10.59	0.246
Systolic BP (mmHg)	157.2±14.29	101.04±9.47	<0.001
Diastolic BP (mmHg)	100.8±7.59	68.0±6.45	<0.001
Serum Magnesium (mg/dl)	1.62±0.16	1.92±0.16	<0.001

p-value< 0.05 is significant.

Table 1. Comparison of BMI between the preeclamptic women and normal pregnant women

Contents	Cases		Controls	
	Mean	S.D	Mean	S.D
BMI	28.71	4.70	22.46	3.42

P < 0.001

From the above result it was evident that p value was significant and the BMI of preeclamptic women was significantly higher than that of the normal pregnant women.

Table 2: Comparison of pulse rate between the preeclamptic women and the normal pregnant women

Content	Cases		Controls	
	Mean	S.D	Mean	S.D
Pulse	97.36	8.58	94.16	10.59

P value = 0.246

From the above result it was evident that the p value was not significant and there was no significant difference in the pulse rate between the cases and the controls.

Table 3: Comparison of Systolic Blood Pressure between the preeclamptic women and the normal pregnant women

Content	Cases		Controls	
	Mean	SD	Mean	SD
Systolic Blood Pressure (mmHg)	157.2	14.29	101.04	9.47

P Value < 0.001

From the above results it was clear that the p value was significant and there was a significant increase in systolic pressure in the preeclamptic women compared to the normal pregnant women.

Table 4: Comparison of Diastolic Blood pressure between the preeclamptic women and the normal pregnant women

Contents	Cases		Control	
	Mean	SD	Mean	SD
Diastolic Blood pressure (mmHg)	100.8	7.59	68.0	6.45

P value < 0.001

From the above results it was clear that there was a significant increase in diastolic blood pressure in the cases when compared to the controls.

Table 5: Comparison of the serum Magnesium levels between the preeclamptic women and the normal pregnant women

Content	Cases		Controls	
	Mean	SD	Mean	SD
Serum Magnesium (mg/dl)	1.62	0.16	1.92	0.16

P value < 0.001

The normal serum magnesium concentration is 1.7–2.4mg/dl. From the above results it is clear that there is a significant decrease in the level of serum magnesium in the women with preeclampsia compared with the normal pregnant women.

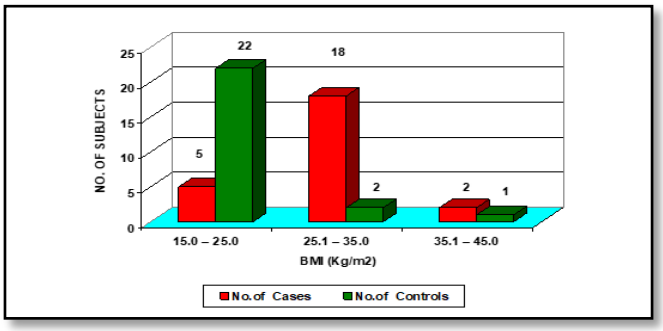

Figure 1: Comparison of BMI between the preeclamptic women and normal pregnant women

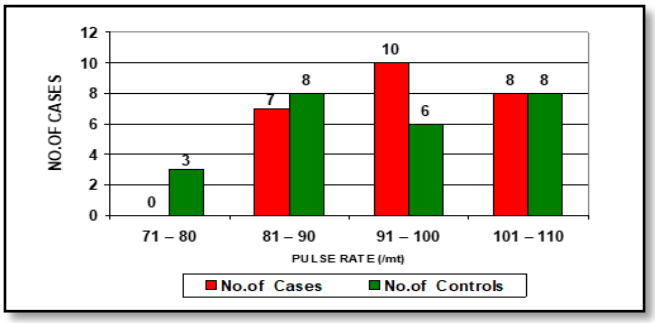

Figure 2: Comparison of pulse rate between the preeclamptic women and the normal pregnant women

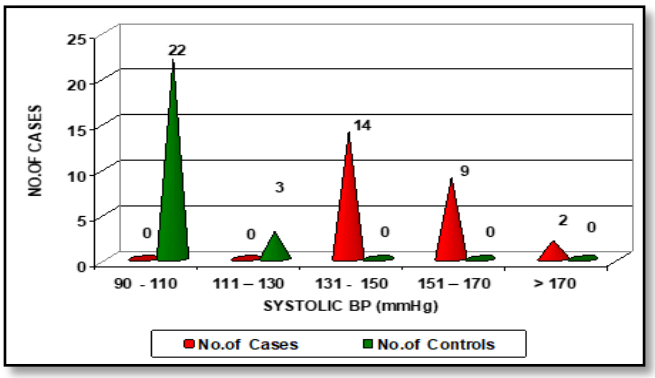

Figure 3: Comparison of Systolic Blood Pressure between the preeclamp-

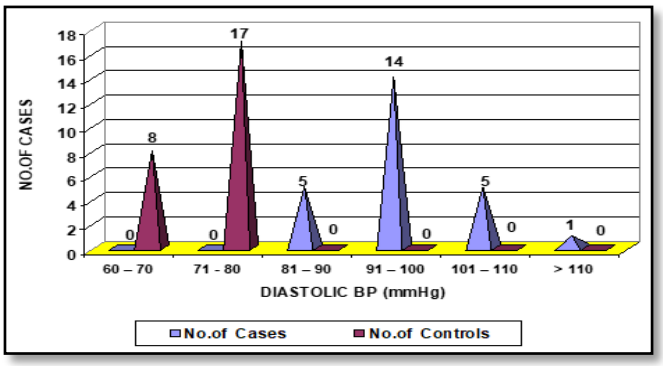

Figure 4: Comparison of Diastolic Blood pressure between the preeclamptic women and the normal pregnant women

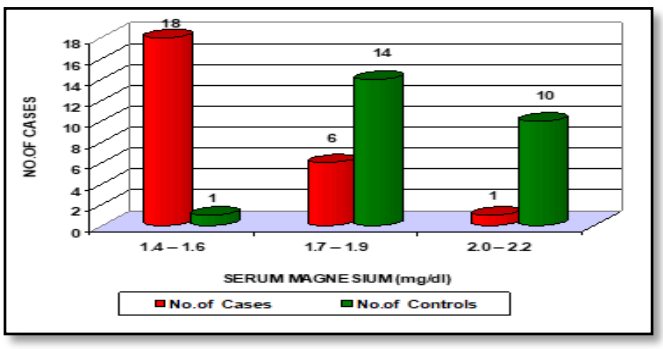

Figure 5: Comparison of the serum Magnesium levels between the preeclamptic women and the normal pregnant women

Statistical Analysis: The comparison between the cases and controls was done by using one - way ANOVA test using SPSS (Statistical Package for Social Science) software, Sigma stat version 3.5. The significance was drawn at p value (probability) of < 0.05.

DISCUSSION

The changes in the levels of serum Magnesium in preeclamptic women compared to the normal pregnant women were studied by several other investigators.

In the present study the Body Mass Index of preeclamptic women is significantly higher than that of the normal pregnant women. These findings are in agreement with the studies of Chanvityapunthumapol et al, 2008[8]. Akinloye et al[2], 2010 in their study showed that there was no significant difference in the BMI between the preeclamptic and the normal pregnant women.In 2001, Pipkin in his study showed that the women with higher BMI become hypertensive than those with lower BMI[21-25].

In the present study there is a significant decrease in the mean serum magnesium concentration in preeclamtic women compared to the normal pregnant women.

Serum magnesium levels have significant effects on the cardiac excitability and reactivity. Magnesium, as a calcium antagonist promotes vascular smooth muscle relaxation. Thus the low levels of magnesium predispose to increase in the arterial pressure. Magnesium deficiency contribute towards placental insufficiency and thus to the

The studies of Idogun et al[18], 2007 andIndumati et al[19], 2010showed that the serum calcium level and magnesium levels in preeclamptic pregnant women is significantly lower than that of the normal pregnant women.

In 2008, Chanvitya et al[8] in his study revealed that the serum calcium level was lower in preeclamptic women when compared with the normal pregnant women but there was no difference in the serum magnesium levels.There was no significant decrease in the mean serum magnesium levels between the preeclamptic and the normal pregnant women in the studies conducted by Golmohammed et al 2008[12].

Studies by Jain S et al[20], 2010 showed that there was a significant reduction in the levels of serum magnesium in the patient with preeclampsia compared with the normal pregnant women.

In the present study no significant correlation could be made between levels of serum Magnesium and the severity of preeclampsia[26-30].

CONCLUSION

In this study the serum Magnesium levels is compared between 25 women with preeclampsia with 25 normal pregnant women in third trimester of the pregnancy.

This study has shown that the serum Magnesium levels in preeclampsia are significantly lower than the normal pregnant women with p value < 0.001.

From the above study, though the magnesium deficiencies cannot be pinpointed as the sole factors for the aetiology of preeclampsia, they have a definite role in the development of preeclampsia. Magnesium deficiency may contribute towards placenta insufficiency and thus to the development of preeclampsia as it contribute to the uterine artery spasm, fetal growth retardation and has a role in prostaglandin synthesis[31,32]. It has been suggested that magnesium supplementation during pregnancy can reduce maternal morbidity and improve fetal outcome.

Conflict of interest

The authors declare that there are no conflict of interests.

Financial disclosure

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