

SERUM MAGNESIUM LEVELS IN MILD AND SEVERE PREECLAMPSIA AND NORMAL PREGNANT WOMENR. Sujatha¹, C. H. Madhuri², K. V. Sudhamadhuri³, T. Radha⁴**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: OBJECTIVE: The aim of this study is to compare serum magnesium levels in women with mild, severe preeclampsia, and normal Pregnant women. **MATERIALS AND METHODS:** The present study was conducted in Victoria Government hospital and King George Hospital Visakhapatnam during the period July 2010-June 2011. The study consists of 50 cases of normotensive uncomplicated pregnant women taken as control and 40 cases of mild preeclampsia, 10 cases severe preeclampsia. The samples were collected from the women attending the Antenatal outpatient clinics and from women who were admitted for treatment and delivery. **SPECIMEN COLLECTION:** On admission, venous serum samples were collected when the patients were in the supine position, prior to their commencement to intravenous therapy. The venous blood was taken from the participant's antecubital vein, placed in a plain vacuum tube. Serum magnesium was measured by colorimetric method by Roche Cobas Integra 800. Other parameters like serum calcium, creatinine, uric acid, fasting blood sugar, and urine sugar and albumin are also measured. The data was analyzed with the SPSS software package version 15.0 and expressed in terms of mean, standard deviation (SD). Continuous variables of serum magnesium concentrations of the three groups were compared by F-test. Maternal and perinatal outcome were analyzed. **RESULTS:** The serum magnesium levels in severe preeclamptic women was significantly lower (1.68 + 0.19 mg/dl vs. 2.1 + 0.206 mg/dl, p = 0.0001; and 1.55 + 0.190 mg/dl vs 1.68+0.19mg/dl, p = 0.059. The study of biochemical parameters shows that, the mean serum magnesium levels in control group is 2.10 +/- 0.21, (normal range 1.8-2.4 mg/dl), in mild cases 1.69 +/- 0.19 and in severe cases 1.58 +/- 0.20. **CONCLUSION:** Preeclampsia is more common in primigravida, younger age group and in low socio economic group. Preeclampsia is associated with increased prematurity rate and low birth weight. Preeclampsia is associated with hypocalcaemia, hypomagnesaemia and hyperuricaemia. **KEYWORDS:** Pregnancy, mild Preeclampsia, severe preeclampsia, Eclampsia, serum magnesium levels, Hypomagnesemia.

INTRODUCTION: Preeclampsia is a pathological condition occurs in pregnancy. It is a pregnancy specific syndrome characterized by new onset of hypertension during pregnancy after 20 weeks and associates with proteinuria. It is classified as mild and severe, depending on the rise of blood pressure and associating features. Normally during pregnancy due to hemodilution and increased renal clearance and consumption of minerals by growing fetus and decreased intake, the magnesium levels are decreased as the pregnancy advances. But in preeclampsia high vasopressin levels and albuminuria have been attributed to the cause of lowering of serum magnesium. There may be a causal relationship since magnesium is involved in blood pressure regulation through an intracellular inhibition of NO synthase in endothelial cells. The extra cellular magnesium concentration influences calcium metabolism of vascular smooth muscle cells by changing the

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calcium influx through the plasma membrane. Consequent to hypomagnesaemia serum calcium also falls which further aggravates the neuromuscular irritability and convulsions. Laboratory studies have suggested that magnesium augments factor IX and VIII activity increases platelet aggregation, and reduces the levels of proteins C and S thus favoring increased haemostatic function. However, other studies have shown magnesium to decrease platelet aggregation, decrease endothelin I levels, and increase antithrombin III levels resulting in suppressed thrombus formation.¹

The fall in serum concentration of magnesium is significant in both mild and severe preeclampsia when compared to control population. Several studies reported hypomagnesaemia in preeclampsia.²

Preeclampsia and eclampsia are pathologic situations responsive to parenteral magnesium treatment. Therapy is based on blocking of acetylcholine at the neuromuscular junction, inhibition of release of catecholamines, and enhancement of the effect of prostacycline / thromboxane ratio. Magnesium sulfate, used for the prevention of seizures in preeclampsia has anticoagulant and antiplatelet effects. It decreases neuromuscular irritability. The incidence of Eclampsia where the preeclampsia is not treated with Magnesium sulphate 1 in 200.³ Preeclampsia is responsible for 15% of premature deliveries.⁴ World-wide preeclampsia is responsible for approximately 14% of maternal deaths (WHO, 2004. Bethesda, MD).

Mild preeclampsia is defined as a blood pressure of at least 140/90 mmHg measured on two occasions 6 hours apart, accompanied by proteinuria of at least 300 mg per 24 hours, or at least 1+ on dipstick testing.

Severe preeclampsia is defined as having one or more of the following criteria: blood pressure of at least 160/110 mmHg measured on two occasions 6 hours apart, proteinuria of at least 5 g per 24 hours, or at least 3+ on dipstick testing, oliguria of lesser than 500 ml per 24 hours, cerebral or visual disturbances, pulmonary edema or cyanosis, epigastric or right upper quadrant pain, impaired liver function, thrombocytopenia and fetal growth restriction.

MATERIALS AND METHODS: The present study was conducted in Victoria Government hospital and King George Hospital Visakhapatnam during the period of one year. The study consists of 50 cases of normotensive uncomplicated pregnant women taken as control and 40 cases of mild preeclampsia, 10 cases severe preeclampsia. The samples were collected from the women attending the Antenatal outpatient clinics and from women who were admitted for treatment and delivery. Inclusion criteria include all pregnant women are at or beyond 28 weeks of gestation, singleton pregnancy, blood pressure of at least 140/90 mmHg measured on two occasions 6 hours apart, and age between 15-40 years. Exclusion criteria include women with chronic hypertension, renal disease, cardio vascular disease, thyroid disease, diabetes mellitus, twin pregnancy, and molar pregnancy.

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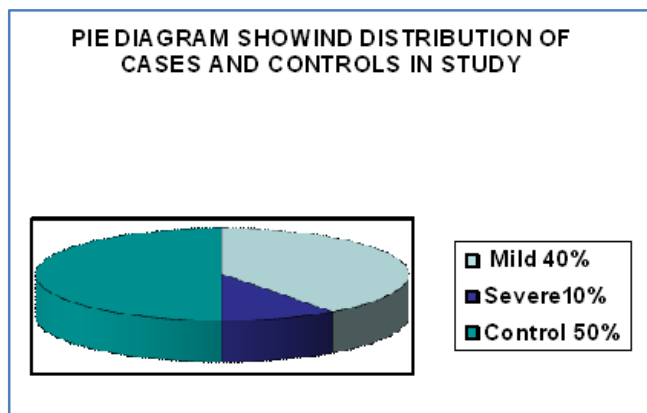


Fig. 1

SPECIMEN COLLECTION: The venous blood was taken from the participant's antecubital vein, placed in a plain vacuum tube. Blood samples were allowed to clot at room temperature and then centrifuged at 2,000 rpm for 7 minutes. Serum aliquots were stored at 2-8 degree Celsius until analysis. Serum magnesium was measured by Calmagnite method. Other parameters like serum calcium, creatinine, uric acid, fasting blood sugar, and urine sugar and albumin are also measured. The data was analyzed with the SPSS software package version 15.0 and expressed in terms of mean, standard deviation (SD). Continuous variables of serum magnesium concentrations of the three groups were compared by F-test. Maternal and perinatal outcome were analyzed.

RESULTS: The serum magnesium levels in severe preeclamptic women was significantly lower (1.68 + 0.19 mg/dl vs. 2.1 + 0.206 mg/dl, $p = 0.0001$; and 1.55 + 0.190 mg/dl vs 1.68+0.19mg/dl, $p = 0.059$). The study of biochemical parameters shows that, the mean serum magnesium levels in control group is 2.10 +/-0.21, (normal range 1.8-2.4 mg/dl), in mild cases 1.69 +/- 0.19 and in severe cases 1.58 +/- 0.20.

In mild preeclampsia out of 40 cases, 15 cases (37.5%) had serum magnesium levels <1.8 mg/dl and 25 cases (67.5%) had serum magnesium levels within the normal range. In severe preeclampsia, the serum magnesium levels in 7 cases (70%) are < 1.8 mg/dl and 3 cases (30%) had normal serum magnesium levels. The fall in serum concentration of magnesium is significant in both mild and severe preeclampsia when compared to control group.

Magnesium levels	Cases of Preeclampsia			Controls
	Mild N (%)	Severe N (%)	Total N (%)	Total N (%)
Less than 1.8 mg/dl	15(37.5)	7 (70)	22 (44)	1 (2)
More than 1.8 mg/dl	25(67.5)	03(30)	28(56)	49(98)
Mean (mg/dl)	1.69	1.55	1.62	2.1
SD	0.19	0.19	----	0.20
SEM	0.030	0.065	-----	0.029

Table 1: Serum Magnesium levels in study groups

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Study group	DBP range mm Hg	No of cases (n)	Mean mm Hg	SEM
Severe	110-125	10	117.5+/- 5.8	1.83
Mild	90-110	40	95 +/-4.56	0.72
Controls	<90	50	75.30+/-5.6	0.79

Table 2: The diastolic blood pressure range in study groups

Parameters	Mild preeclampsia	Severe preeclampsia	Controls
Mean Age (years)	22.50	23.80	22.92
DiastolicBP(mmHg)	96.50	113.50	75.30
S.Calcium(mgs/dl)	8.660	7.840	9.406
S.Uric acid(mgs/dl)	5.498	6.500	5.064
S.Creatinine(mgs/dl)	0.993	1.580	0.744
Blood sugar (mgs/dl)	76.94	76.94	72.54
Gestational age(wks)	37.45	35.30	38.5
Fetal weight (kgs)	2.68	2.15	2.866

Table 3: Mean values of other clinical and other biochemical parameters in population distribution

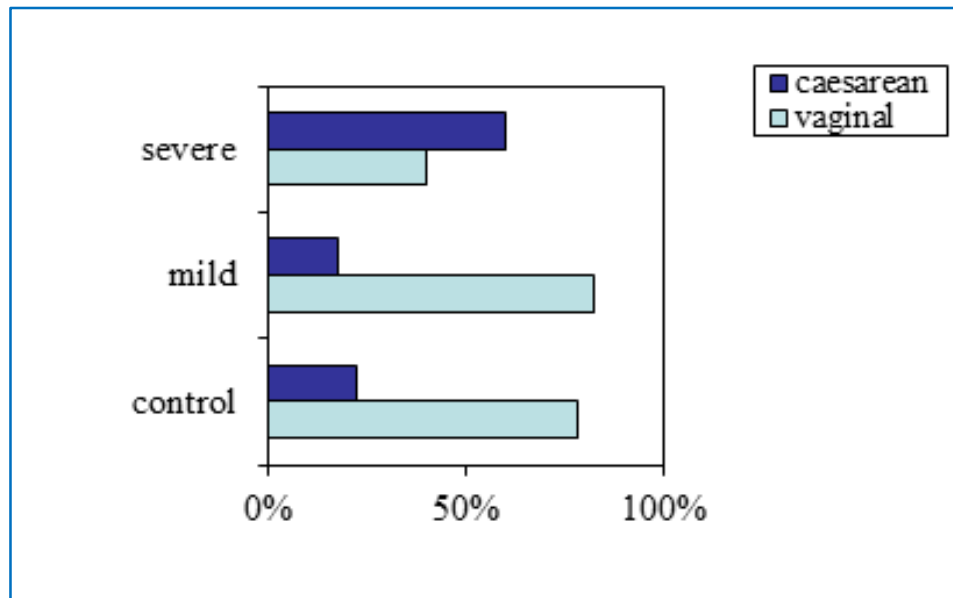


Fig. 2: Mode of delivery in study groups

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Complication	Cases of Preeclampsia			Controls
	Mild N (%)	Severe N (%)	Total N (%)	Total N (%)
Imminent signs	1 (2.5)	4 (40)	5 (10)	0
Eclampsia	1 (2.5)	3 (30)	4 ((8)	0
Renal failure	0 (0)	1 (10)	1 (2)	0
Neurological	0 (0)	1 (10)	1 (2)	0
Death	0 (0)	0 (0)	0 (0)	0

Table4: Maternal out come in relation to the severity of disease

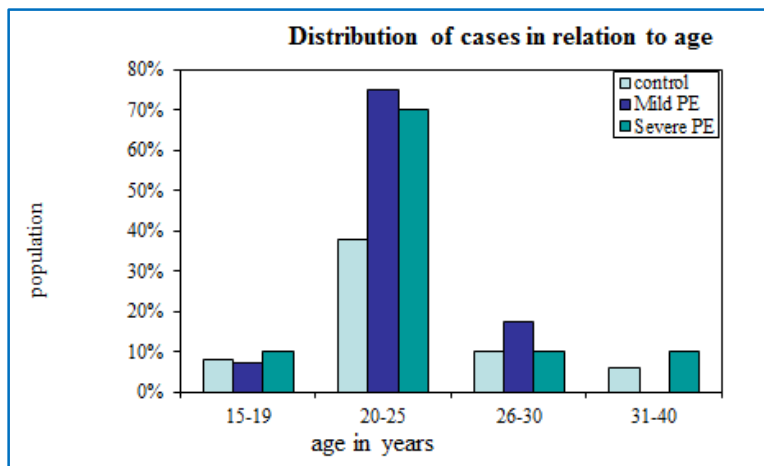


Fig.3

In the present study the mean age of the women is 22.92 years, 22.50 years, 23.8 years in control group, mild preeclampsia and in severe preeclampsia respectively.

The mean gestational age is 38.5weeks in control group, 37.45 weeks in milder group 35.30 weeks in severe disease.

The diastolic pressure in severe group is 115.5mm Hg and 96.50 mmHg in mild Preeclampsia. The serum concentration of calcium in control group is 9.40mg/dl in mild cases is 8.66mg/dl and in severe cases 7.84mg/dl. The fall in serum concentration of calcium is significant in severe preeclampsia when compared to normal and mild eclampsia. The mean serum uric acid levels in control group is 5.1mg/dl in mild preeclampsia is 5.49mg/dl and severe cases is 6.5 mg/dl. The mean serum uric acid levels in mild cases is slightly increased and significantly increased in severe cases. The mean serum levels of creatinine in control group are 0.75mg/dl and in mild cases 0.99mg/dl and in severe cases is 1.5mg/dl. The serum creatinine levels are significantly increased in severe preeclampsia when compared to mild and control group. The mean blood sugar levels in all three groups are within normal limits with no significance. The average fetal weight in Indian population is 2.8 kg. The mean weight of the newborn in control, group, mild preeclampsia and in severe preeclampsia is 2.9 kg, 2.7 kg, 2.1 kg respectively.

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DISCUSSION: In present study the magnesium levels were low in only one third of mild preeclamptic group women and two thirds have normal magnesium levels. But in severe form of preeclampsia low magnesium levels were seen in more than half of the women. Only three women with preeclampsia have the magnesium levels within normal limits. The women with very low levels of magnesium presented with imminent signs of eclampsia. And also a woman with convulsions had very low levels of magnesium. The lower limit of magnesium level is 1.2mg/dl. In control group all women have the normal limits of magnesium levels ie 1.8-2.4 mg/dl except in one with low level of magnesium levels.

Study group	Mean mg/dl			SD			P value		
	Control	mild	severe	Control	mild	severe	Control	mild	severe
Seemajain Et al(2008)	1.92	1.63	1.51	0.32	0.34	0.27	---	---	---
Vahidrodsari ⁵ Et ai 2008	2.29	1.92	---	0.69	0.37	---	---	<0.001	---
Bunyamin ⁶ et al 2008	1.86	1.63	---	0.05	0.05	----	<0.001	<0.001	----
Punthumapol et al 2008	2.04	2.04	2.24	0.19	0.21	0.62	--	<0.001	<0.001
Sukonpan. ⁷ K Et al 2005	2.07	1.87	---	0.22	0.19	---	---	<0.001	---
J.Chaudhuri et al 2003	1.98	1.39	1.23	0.08	0.08	0.06	--	<0.001	<0.001
Presentstudy 2010	2.10	1.68	1.55	0.20	0.19	0.19	---	<0.001	<0.001

Table 5: Comparison of mean values of magnesium with other similar studies

The magnesium level in pregnant women in control group, mild preeclampsia severe preeclampsia are 2.10+/-0.21 mg/dl, 1.68+/-0.2mg/dl, 1.55+/-0.21 mg/dl respectively. The other studies showed similar changes in the magnesium levels which are correlating with preeclampsia. In a study of Seemajain et al 2008 and J. Chaudhuri et al 2003 showed the magnesium levels are in severe preeclampsia 1.51+/-0.27 mg/dl, 1.23+/-0.08, in mild preeclampsia 1.63+/-0.34, 1.39+/-0.08 mg/dl and in control 1.92+/-0.32, 1.98+/-0.08 mg/dl respectively. This indicates there is significant hypomagnesaemia in mild and severe eclampsia⁸. Conversely the study of Punthumapol et al 2008 shows the magnesium levels in severe preeclampsia 2.24 +/-0.19mg/dl, in mild preeclampsia and control group the level is 2.04 +/- 0.19. Here hypermagnesaemia in severe preeclampsia is noted which contradicts the present study.⁹

Several other studies also reported hypomagnesaemia in preeclampsia. And also hypomagnesaemia is associated in normal pregnant women due to hemodilution.¹⁰ Generally, magnesium has been known as an essential cofactor for many enzyme treatment. Besides the serum magnesium, the hyperuricemia is believed to result from the decreased renal excretion that occurs as a consequence of the preeclampsia but this result is probably also increased production secondary to tissue ischemia and oxidative stress. Soluble uric acid impairs nitric oxide generation in endothelial cells. Hyperuricemia induces endothelial dysfunction and may induce hypertension and vascular disease. Therefore, the modification of calcium, magnesium and uric acid metabolism during pregnancy could be one of the potential causes of preeclampsia. However, the role and status of

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serum calcium, serum magnesium and serum uric acid in pregnant women are still being discussed. systems. It also plays an important role in neurochemical transmission and peripheral vasodilatation. Magnesium sulfate appears to be safe and effective for the prevention of seizures and has been used as the drug of choice in severe preeclampsia and eclampsia.

The implications of the magnesium deficiency during pregnancy include the speculations that lower magnesium levels increase the uterine contractility. Evidence suggests that the serum magnesium levels are lower in women with preterm labor. Magnesium levels are also lower in spontaneous abortions in first trimester and in pregnant diabetic women. It is possible that an electrolyte imbalance may predispose the women with low magnesium levels to devastating complications of preterm delivery and preeclampsia. Hypomagnesaemia may be due to the development of insulin resistance. Pregnancy is associated with decrease in peripheral insulin sensitivity primarily by third trimester. In women with preeclampsia an insulin resistant syndrome is apparent.¹¹ The most of the women with mild and severe preeclampsia from the below poverty group correlating with malnutrition causing anaemia, folic acid, vitamin C deficiency, magnesium, calcium deficiencies, lack of proper antenatal care, screening for preeclampsia etc.¹² As nutrition has long been hypothesized to have a role in the etiology of preeclampsia periconceptional exposures may be relevant, as they may affect implantation and/or decidual vascular remodeling.

The investigators found that intakes of vitamin C, fruits, and vegetables below recommended values were associated with an increased risk of preeclampsia. Lisa M et al observed that regular use of multivitamins in the periconceptional period was associated with a 45 percent reduction in preeclampsia risk. And a protective effect confounding by fruit and vegetable intake, which suggested a 37 percent reduction in risk, supported these findings.¹³

CONCLUSION: Preeclampsia associates with hypomagnesemia. It is more common in primigravida, younger age group and in low socio economic group. Preeclampsia is associated with increased prematurity rate and low birth weight. Preeclampsia is associated with hypocalcaemia, hypomagnesaemia and hyperuricaemia.

REFERENCES:

1. Sekiya F, Yoshida M, Yamashita T, Morita T. Magnesium (II) is a crucial constituent of the blood coagulation cascade. *J BiolChem* 1996; 271: 8541-4.
2. Kisters K, Barenbrock M, Louwen F, Hausberg M, Rahn KH, Kosch M. Membrane, intracellular, and plasma magnesium and calcium concentrations in preeclampsia. *Am J Hypertens* 2000; 13: 765-9.
3. Royal College of Obstetricians and Gynaecologists (2006).
4. Goldenberg Goldenberg RL, Rouse DJ. Prevention of premature birth. *N Engl J Med.* Jul 30 1998; 339(5): 313-20.
5. Vahidrodsari F, , Tourabizadeh A, , Esmaeli H, Shahabian M, et al. Serum Calcium and Magnesium in Preeclamptic and Normal Pregnancies; A Comparative Study. *J Reprod Infertil.* 2008; 9(3): 257.
6. Bunyamin Boekci, Mine Gulaboglu and Mustafa Gul, Biological trace elements Reasearch volume 129,numbers 1-3, 1-8 DOI: 10.1007/s12011-008-8278-5.

ORIGINAL ARTICLE

7. Sukonpan K, Phupong V Arch Gynecol Obstet 2005 Nov; 273(1):12-6. Epub 2005 Oct 28. PMID: 15480721.
8. Seema Jain, Priyamvada Sharma, ShobhaKulshreshtha, Govind Mohan and SarojSingh Biological Trace Element Research Volume 133, Number 2, 162-170, DOI:10.1007/s12011-009-8423-9.
9. Punthumapol C, Kittichotpanich BJ Med Assoc Thai 2008 Jul; 91(7):968-73. PMID: 18839833.
10. Kurzel American Journal of Perinatology [1991, 8(2): 119-12.
11. Kaaja Semin Reprod Endocrinol. 1998; 16(1): 41-6.
12. [Best Evidence] Villar J, Purwar M, Merialdi M, Zavaleta N, Thi Nhu Ngoc N Anthony J, et al. World Health Organisation multicentre randomised trial of supplementation with vitamins C and E among pregnant women at high risk for pre-eclampsia in populations of low nutritional status from developing countries. BJOG. May 2009; 116(6): 780-8.
13. Lisa M. Bodnar Gong, Tang, Roberta B. Ness, Gail Harger, James M. Roberts American Journal of Epidemiology Volume 164, Issue 5 Pp. 470-477.

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