EVALUATION OF SERUM MAGNESIUM AND CALCIUM IN THE PREDICTION OF PREECLAMPSIA IN AT RISK MOTHERS

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CERTIFICATE

This is to certify that this dissertation entitled **"EVALUATION OF SERUM MAGNESIUM AND CALCIUM IN THE PREDICTION OF PREECLAMPSIA IN AT RISK MOTHERS"** is a bonafide work done by **Dr.R. NIRMALA** post graduate student in **M.D. (OBSTETRICS AND GYNAECOLOGY)** under my over all supervision and guidance at The Institute of Social Obstetrics and Government Kasturba Gandhi Hospital, Madras Medical College, Chennai in partial fulfillment of the regulations of Tamilnadu Dr.M.G.R. Medical University for the award of M.D. Degree in Obstetrics and Gynaecology.

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CONTENTS

INTRODUCTION

Preeclampsia is a disease with worldwide significance to mothers and infants and it is a leading cause of death and disability in mothers and infants.[1,2] This disorder was first recognized almost 2000 years ago. Celsus described pregnant women with seizures that abated with delivery. This disorder was termed eclampsia and for 2000 years, was considered a pregnancy specific seizure disorder.

In the late 1800's the association of, initially, proteinuria and later increased blood pressure with eclampsia was recognized. It was also noted that increased blood pressure and urinary protein antedated seizures. From this came the term pre-eclampsia (Chesley, L.C. 1978).[3]

According to WHO estimates, about 510,000 maternal deaths (about 0.9 percent of total deaths) occurred globally during the year 2002, of these deaths about 1,71,000 were in South East Asian Countries.[4] Most of the maternal deaths are preventable. The life-time chances of maternal death in the world as a whole is 1 in 75. It

varies from region to region and from country to country. In India, the life-time risk of maternal death for mother is 1 in 61.[5,6,7]

Estimates of Maternal Mortality in some countries are given below

ESTIMATES OF MATERNAL MORTALITY[7,8]

Country	**Maternal Mortality (Per 1,00,000 live births)**
India	307
Srilanka	92
Bangladesh	380
Nepal	740
Myanmar	360
Thailand	44
China	56
Japan	10
Singapore	15
U.K.	11
USA	14
Switzerland	7

Causes of maternal death worldwide are Obstetric Haemorrhage 25%, Infection 15%, Eclampsia 12%, Obstructed labour 8%, Unsafe Abortion 13%, Other direct causes 8%, Indirect causes 20%.

Most common causes of Maternal death in India (2006)[9] are Haemorrhage 29%, Anemia 19%, Sepsis 16%, Obstructed labour 10%, Abortion 9%, Toxemia 8% and others 9%.

The current maternal mortality ratio in Tamil Nadu (2006) is 92/100,000 live births. (NFHS III)[10]

For many years diet has been suggested to play a role in pre-eclampsia.[3] Nutritional deficiencies of both macro and micronutrients are common in women of reproductive age group in developing countries. Epidemiological and biological evidence suggest that acute or chronic specific nutritional deficiencies can contribute to severe maternal morbidity.

A role of altered calcium metabolism in the pathogenesis of pre-eclampsia has been suggested based on epidemiological

evidence linking low dietary levels of calcium and increased incidence of the disease.[11,12]

Magnesium is one of the essential minerals needed by humans in relatively large amounts. Dietary surveys during pregnancy consistently demonstrate that many women, especially those from disadvantaged backgrounds, have intakes of magnesium below the recommended levels. Observational studies from medical records reported that magnesium supplementation during pregnancy was associated with reduced risk of pre-eclampsia.[12]

In this above background, it is desirable to know the serum levels of magnesium and calcium in Indian pregnant women. It may give some clue whether routine monitoring of serum magnesium and calcium may have potential in the a) early detection of pregnant women at risk of pre-eclampsia[13] b) monitoring the progress of diverse therapeutics during clinical management[14] or c) Prophylactic calcium and Magnesium supplementation during pregnancy could be recommended.[15]

REVIEW OF LITERATURE

Sukonpan K, Phupong V[16] conducted a study with the aim of measuring serum levels of calcium and magnesium in pre-eclamptic pregnancies and to compare them with those in normal pregnancies. Venous serum samples were collected from 40 preeclamptic women and 40 normal pregnant women. The blood samples were analyzed for calcium and magnesium. The results were statistically analyzed. The serum calcium concentration in pre eclamptic pregnant women is significantly lower than that in normal pregnant women (9.0 ± 0.14 mg / dl vs 9.7 ± 0.7 mg / dl, P < 0.0001). Like serum calcium, serum magnesium concentration in preeclamptic women is significantly lower than that in normal pregnant women (0.77 ± 0.08 mmol/L vs 0.85 ± 0.09 mmol/L, P = 0.001).

The conclusion of the study is that both serum calcium and serum magnesium levels in preeclamptic pregnant women are lower than in normal pregnant women.

SR Ambwani, UH Shah et al.,[15] conducted a prospective case controlled study to find out the role of electrolytes, (magnesium and calcium) in the pathophysiology of hypertension during pregnancy.

The serum magnesium concentration in preeclamptics were lower than the normotensive pregnant women (1.34 ± 0.06 meq/L, Vs 2.06 ± 0.67 meq/L, $P < 0.001$). The serum calcium concentration in preeclamptics were lower than the normotensive pregnant women (7.76 ± 0.37 mg/dl Vs 9.24 ± 0.15 mg/dl $P < 0.01$). Findings from this study showed a significant decrease in serum level of magnesium and calcium in preeclamptic women.

Qi Q, Li W et al.,[17] evaluated the magnesium and calcium concentrations of serum in patients with Pregnancy Induced Hypertension. 26 patients with Pregnancy Induced Hypertension and 27 healthy women in their late pregnancy were studied. The serum magnesium and calcium contents were measured. When compared with healthy women in their late pregnancy, the serum magnesium and calcium contents in patients with Pregnancy Induced Hypertension decreased significantly ($P < 0.01$ and $P < 0.05$).

Kisters K, Barenbrock M et al.,[18] studied the changes in calcium and magnesium metabolism in normal pregnancy and pre eclampsia. Plasma, intracellular and membrane calcium and magnesium concentrations were determined. Twenty five controls, 18 untreated healthy pregnant and 16 nullipara preeclamptic

women were investigated. Plasma, intracellular magnesium concentration were significantly lower in the preeclamptic group as compared to controls ($P < 0.01$). The erythrocyte membrane magnesium content was found to be significantly decreased in the preeclamptic women as compared to healthy subjects ($P < 0.001$). There was a significant decrease in the plasma calcium concentration in the preeclamptic group compared to controls or healthy pregnant women ($P < 0.05$). Membranous calcium content was significantly increased in the preeclamptic group versus controls or healthy pregnant women ($P < 0.001$) and an inverse correlation with membranous magnesium content was found ($r = -0.79$, $P < 0.01$). Lowered plasma, intracellular and membrane magnesium concentrations in preeclamptic may contribute to the development of hypertension in pregnancy. In addition, a disturbed calcium homeostasis is observed in preeclampsia.

Kisters K, Louwen F et al,[19] investigated the changes in calcium and magnesium metabolism in normal pregnancy and pre eclampsia. Plasma calcium and magnesium concentrations were determined. 22 untreated healthy pregnant women and 20 preeclamptic women were investigated. In each patient, plasma calcium and magnesium contents were measured. The results of

the study are plasma magnesium concentration was significantly lowered in preeclamptic group as compared to control subjects ($P < 0.0001$). There was a significant decrease in the plasma calcium concentrations of the preeclamptic group as compared to healthy pregnant women, ($P < 0.05$). Additionally, a disturbed calcium homeostasis is observed in preeclampsia.

Sulaiman S, Adeeb N et al.,[20] determined total calcium, total magnesium in pregnant normotensive, pregnancy induced hypertension and preeclampsia women. Total calcium levels were of lower levels ($P < 0.05$) in pregnancy induced hypertension women and preeclampsia women compared to normotensive pregnant women.

Huang Y, Zhang W et al., [21] studied magnesium and calcium levels of plasma before and after magnesium sulfate treatment in patients with pregnancy induced hypertension. The calcium and magnesium levels in plasma of 36 patients with PIH and 14 healthy gravidi in their late pregnancy were determined and the calcium and magnesium levels after 4 hours infusion of magnesium sulphate also were determined.

The results of the study is plasma calcium and magnesium decreased significantly in moderate and severe Pregnancy Induced Hypertension patients. After magnesium sulphate infusion for Pregnancy Induced Hypertension, magnesium and calcium levels in plasma increased. The conclusion of the study is that magnesium deficiency is the basis of calcium and magnesium disturbances in PIH, and magnesium sulphate treatment may improve the situation effectively.

Kumru S, Aydin S et al.,[13] did a comparative study of serum calcium and magnesium levels in preeclamptic and healthy pregnant women. Samples were collected from 30 pre eclamptic and 30 healthy pregnant women. The serum calcium levels were lower in the preeclamptic women ($P < 0.001$), whereas the serum magnesium concentration showed statistically insignificant differences between the two groups. Measurement of these elements may be useful for the early diagnosis of preeclampsia.

Smolarczyk R, Romejko et al.,[22] studied serum concentrations of calcium and magnesium in women with pregnancy induced hypertension. Study group consisted of 63 women in the III trimester of pregnancy, 32 subjects with Pregnancy Induced Hypertension (investigated group) were compared to control group

consisted of 30 healthy patients with uneventful course of gestation. Concentrations of calcium and magnesium in serum were determined. It was stated that due to renal impairment observed during Pregnancy Induced Hypertension, calcium urine excretion and calcium concentration in serum decreased in the course of Pregnancy Induced Hypertension.

Standley CA, Whitty JE et al., [23] did a study to compare the serum levels of ionized and total magnesium and ionized calcium and total calcium over the course of pregnancy in normal pregnant women and in women who develop pre eclampsia. Venous serum samples from 31 pregnant women during their first, second and third trimesters were collected. Samples were analyzed for ionized and total magnesium, ionized and total calcium. In 22 normal pregnant women, both serum ionized and total magnesium levels decreased significantly with increasing gestational age. No changes in ionized or total calcium were observed. Nine of the 31 subjects developed pre eclampsia by term; serum total magnesium levels decreased significantly by the second trimester in these women compared with those of normal pregnant women. Their results provide evidence of decrease in ionized and total magnesium levels with increasing gestational age during normal pregnancy, as well

as evidence of a magnesium deficiency in women who later develop preeclampsia.

Zhao F.,[24] studied calcium and magnesium contents of the maternal serum in women with pregnancy induced hypertension. Calcium and magnesium in the maternal serum were measured in 106 patients suffering from Pregnancy Induced Hypertension and 106 controls (normal pregnant women). Mean maternal serum values of Calcium and Magnesium in the PIH group were 2.46 mmol/L, 0.839 mmol/L respectively and were compared with the corresponding values of 2.765 mmol/L, 0.834 mmol/L in the controls. The calcium levels were lower in the PIH group ($P < 0.05$ or $P < 0.01$). This study suggests that maternal serum calcium levels are related to Pregnancy Induced Hypertension and calcium might have a causal role in the development of Pregnancy Induced Hypertension.

Isezuo SA, EKele BA.,[25] did a study to determine if eclampsia is associated with low serum calcium. Serum calcium and magnesium were compared among 30 intrapartum eclamptics and 30 age, parity and gestational age matched women with uncomplicated pregnancy. Serum calcium levels were significantly lower among eclamptics than controls (2.0 ± 0.4 mmol/L, Vs $2.3 \pm$

0.2 mmol/L, P < 0.05). The eclamptics had higher frequency of hypocalcaemia than the controls (40% Vs 6.6%; OR = 14, 95% CI = 1.58 – 316.9, P = 0.01). Serum magnesium levels were similar between the two groups. The conclusion of the study is eclampsia is associated with maternal hypocalcaemia.

Malas NO, Shurideh ZM [26] did a study to determine whether there is difference between the serum calcium of preeclampsia and normal pregnancy. Eighty pregnant women were enrolled in this study, 50 women represented the study group (Pregnancy – induced hypertension), and 30 women represented the control group (normal pregnancy). This study was carried out between March 1998 and February 2000 at King Hussein Medical center, starting from the first or 2nd trimesters and once the patient developed hypetension for the first time in the III trimester. The mean serum total calcium of the study group was (8.22 ± 0.12 mg%). While the mean serum total calcium of the control group was (9.50 ± 0.16 mg %). The result was statistically lower in the study group (P < 0.005). The conclusion of the study is that it has been widely documented that there is a relationship between low calcium level and pregnancy induced hypertension. Therefore

calcium supplementation during late pregnancy may be used to help in the prevention of this disorder.

Hassan TJ, Sadaruddin A et al.,[27] did a study to compare the serum levels of Calcium in preeclampsia and normal pregnant women. They determined serum calcium in 100 normal pregnant women and 50 patients with pre-eclampsia. Serum calcium levels were signficantly lower in patients with pre-eclampsia. Low levels were found as early as 28 weeks and can therefore be used for early diagnosis of preeclampsia.

Kosch M, Hansberg M et al., [28] did a study to compare plasma calcium of patients with pre-eclampsia. 18 untreated, healthy pregnant women and 16 pregnant nulliparous women with manifest pre-eclampsia were included. Plasma calcium concentrations were significantly lower in pre-eclamptic women (1.96 ± 0.l5 mmol/L, $P < 0.01$) compared to women with uncomplicated pregnancies (2.20 ± 0.10 mmol/L).

Gao S, Liu G et al.,[29] did a study to analyse the metabolism of serum calcium in patients with pregnancy induced hypertension. 37 patients with obvious pregnancy induced hypertention, 56 normal pregnant women in the same age groups were tested on

their serum calcium. Results indicated that the respective means of serum calcium levels were statistically lower ($P< 0.05$) than that of normal pregnant women. It was also confirmed that calcium metabolism of patients with pregnancy induced hypertension was obviously abnormal.

PREECLAMPSIA

Preeclampsia is a disorder of unknown etiology. It is a clinical syndrome rather than a single disease. Therefore the pathophysiologic abnormalities of this syndrome are heterogenous and varies among predisposed women.

According to the working Group of the NHBPEP 2000 hypertensive disorders complicating pregnancy is classified as follows:[30]

1. Gestational Hypertension

   (formerly Pregnancy induced hypertension that included transient hypertension)

2. Preeclampsia

3. Eclampsia

4. Preeclampsia superimposed on chronic hypertension

5. Chronic hypertension

DEFINITION

Gestational Hypertension

- BP ≥ 140 / 90 mm Hg for first time during pregnancy.

- No proteinuria
- BP returns to normal < 12 weeks' postpartum.
- Final diagnosis made only postpartum
- May have other signs or symptoms of preeclampsia.

Preeclampsia

Minimum criteria

- BP ≥ 140 / 90 mm Hg after 20 weeks' gestation
- Proteinuria ≥ 300 mg / 24 hours or ≥ 1 + dipstick

Increased certainty of preeclampsia

- BP ≥ 160 / 110 mmHg
- Proteinuria 2g/24 hours or ≥ 2 + dipstick
- Serum creatinine > 1.2 mg / dl unless known to be previously elevated.
- Platelet < 1,00,000 / mm^3
- Microangiopathic hemolysis (increased LDH)
- Elevated ALT or AST

- Persistent headache or other cerebral or visual disturbance.

- Persistent Epigastic pain.

Eclampsia

- Seizures that cannot be attributed to other causes in a women with preeclampsia.

Superimposed preeclampsia on Chronic hypertension

- New onset proteinuria ≥ 300 mg / 24 hours in hypertensive women but no proteinuria before 20 weeks' gestation.

- A sudden increase in proteinuria or blood pressure or platelet count < 100, 000 / mm^3 in women with hypertension and proteinuria before 20 weeks' gestation.

Chronic Hypertension

- BP ≥140 / 90 mmHg before pregnancy or diagnosed before 20 weeks' gestation not attributable to gestational trophoblastic disease (or)

- Hypertension first diagnosed after 20 weeks' gestation and persistent after 12 weeks' postpartum.

ACOG CLASSIFICATION OF HYPERTENSION DURING PREGNANCY

1. **Pregnancy induced hypertension**

    1.1 Transient Hypertension

    1.2 Preeclampsia

        a) Mild

        b) Severe

    1.3 Eclampsia.

2. **Pregnancy aggravated hypertension**

    2.1 Superimposed preeclampsia

    2.2 Superimposed Eclampsia

3. Coincidental hypertension

INCIDENCE

Incidence of preeclampsia is 5 – 8%.[31] In India the incidence is 7–9%. In The Institute of Social Obstetrics and Government Kasturba Gandhi Hospital the incidence is around 8 – 9%.

RISK FACTORS FOR PREECLAMPSIA

Primigravida

Increasing maternal age[32]

High altitude[33]

Low socioeconomic status

Chronic hypertension

Multiple gestation[34]

Obesity[35]

Factors with reduced risk of Hypertension

Smoking[36]

Placenta Previa[37]

Hypertension

Hypertension during pregnancy is diagnosed when the resting blood pressure is 140/90 mmHg or greater; Korotkoff phase

V is used to define diastolic pressure (Brown MA and Buddle ML 1998; Perry IJ, 1996).[38,39]

Edema

Edema is abandoned as a diagnostic criteria, because it occurs in too many normal pregnant women to be discriminant.[40]

Proteinuria

Proteinuria is an important sign of preeclampsia. Chesley, 1985[41] concluded that the diagnosis of preeclampsia is questionable in its absence. Significant proteinuria is defined by 24 hour urinary protein exceeding 300 mg per 24 hours or persistent 30 mg / dl (1+ dipstick) in random urine samples. Proteinuria is a sign of worsening hypertensive disease.[42]

Proteinuria is assessed by dipstick method.

Protein	Trace	0.1 gm / L
	1+	0.2 gm / L
	2+	1 gm / L
	3+	3 gm / L
	4+	10 gm / L

INDICATORS OF SEVERITY OF HYPERTENSIVE DISORDERS OF PREGNANCY

Abnormality	Mild	Severe
Diastolic BP	< 100 mm Hg	110 mm Hg or higher
Proteinuria	Trace to 1+	Persistent 2+ or more
Headache	Absent	Present
Visual Disturbance	Absent	Present
Upper Abdominal Pain	Absent	Present
Oliguria	Absent	Present
Convulsion	Absent	Present
Serum Creatinine	Normal	Elevated
Thrombocytopenia	Absent	Present
Liver Enzymes elevation	Minimal	Marked
Fetal growth restriction	Absent	Present
Pulmonary edema	Absent	Present

ETIOLOGY

According to sibai 2003, currently plausible potential causes include the following :

1. Abnormal Trophoblastic Invasion[43, 44]
2. Immunological Factors[45,46]
3. Vasculopathy and Inflammatory changes[47]
4. Nutritional Factors[48]
5. Genetic Factors[49, 50]

Pathogenesis

Vasospasm is the basic pathophysiology of preeclampsia.[51]

Endothelial cell activation has become the centerpiece in the contemporary understanding of the pathogenesis of preeclampsia.[52]

Increased pressor responses with alteration in the prostaglandins, Nitric oxide, Endothelins and Angiogenic factors.

Other Systemic Effects of Preeclampsia

Brain	-	edema, hemorrhage, infarction
Eyes	-	serous retinal detachment, cortical blindness, pappiledema
CVS	-	hypertension, pulmonary edema.
RS	-	pulmonary edema, aspiration pneumonia.
Liver	-	congestion, hemorrhage, infarction, rupture.
Kidney	-	glomerulo endotheliosis, nephritic syndrome, acute renal failure.
Blood	-	thrombocytopenia, microangiopathic hemolytic anemia, DIC.
Reproductive	-	IUGR, prematurity, placental abruption, fetal demise.
Skin	-	edema, petechiae, ecchymosis.
Mucosa	-	laryngeal edema.

Predictors of Preeclampsia

1. An elevated blood pressure in mid pregnancy.
2. Roll over test at 28 – 32 weeks
3. Angiotensin sensitivity test
4. Measuring micro albuminuria
5. Elevated serum uric acid levels
6. Elevated serum Fibronectin levels
7. Combined first – trimester serum levels of Placental Growth Factor (PIGF) and Soluble fms like tyrosine kinase - 1 (sFlt1).
8. Screening for Fetal DNA in maternal serum during earlier pregnancy may be predictive of subsequent preeclampsia.
9. Uterine artery doppler velocimetry.

MAGNESIUM

Magnesium is the fourth most abundant cation in the body and the most abundant intracellular cation after potassium[53, 54]. The adult human body contains approximately 20 to 28 grams of which 60% is found in bone, 26% in muscle and 13% in soft tissue and < 1% is in blood.[55]

Pharmacokinetics

Normal serum levels are usually in the range 1.8-3 mg/dl (0.48 - 1.05 mmol/L). About half the magnesium in plasma is free, approximately one third is bound to albumin; and the remainder is complexed with citrate, phosphate or other ions.

Magnesium is essential to life. Magnesium plays a role in more than 300 enzymatic reactions and is critically involved in energy metabolism, glucose utilisation, protein synthesis, fat synthesis and breakdown, ATPase functions and virtually all reactions.[56] Magnesium is involved in maintaining cellular ionic balance through its association with sodium, potassium and calcium[57].

It is absorbed in the ileum and colon, absorption decreases as intake increases. The rate of absorption varies from 35 - 45%. Absorbed by two mechanisms, facilitated and simple diffusion. The efficiency of absorption varies with the magnesium status of the individual and the amount of magnesium in the diet. Vitamin D has no effect on magnesium absorption. Parathyroid hormone appears to be essential for both gastro intestinal and renal tubular reabsorption of magnesium. Only 3-5% of filtered magnesium appears in urine, the rest is reabsorbed. Renal impairment may cause magnesium retention and leads to toxicity.

Many calcium channels are magnesium dependant. Higher intracellular magnesium concentrations inhibit calcium transport into the cell and from the sarcoplasmic reticulum. Therefore, in magnesium deficiency, intracellular calcium levels rises significantly. Magnesium deficiency may result in reduced intracellular levels of ATP and potassium and increased intracellular levels of sodium and calcium.

Patient with hypomagnesemia often have calcium deficiency that does not respond to calcium repletion until the magnesium deficiency is addressed.[58] While this phenomenon is partially explained by calcium-magnesium exchange, the primary factor

involved appears to be parathyroid hormone, since magnesium deficiency impairs both the release of parathyroid hormone and its uptake by bone and skeletal end organ.[59]

Magnesium deficiency

Magnesium deficiency refers to depletion of total body stores, while hypomagnesemia describes low serum concentrations < 1.23 mg/dl (< 0.5mmol/L) serum levels can be normal in the presence of low intracellular stores.

In patients with acidosis, magnesium shifts from the intracellular space to extracellular space. While in alkalosis, magnesium shifts from the extracellular space to the intracellular space.[60] Therefore, alkalotic patients may have low serum magnesium levels without total body magnesium deficiency, while those with acidosis may have normal serum levels despite deficient intracellular stores.

Magnesium and Pregnancy

Human pregnancy is characterized by several cardiovascular changes, among them a 50% increase in cardiac output, decrease in systemic vascular resistance, a 40% blood volume expansion, a decrease in mean arterial blood pressure and a 10-15 beats/min

increase in heart rate. It is possible that alterations in magnesium metabolism may be responsible for some of the physiological changes seen during pregnancy and in many disease related to cardiovascular abnormalities. Magnesium has been used extensively in obstetrics for the treatment of alteration of uterine contractility (Premature labor) or increased neuronal and vascular smooth muscle activity (pre-eclampsia).[61]

Electrolyte deficiencies

Patients with electrolyte deficiencies are at increased risk of magnesium deficit. Measuring serum magnesium in hospitalised patients with one electrolyte abnormality detected hypomagnesemia in 42% of hypokalemic patients, 29% of those with hypophosphatemia, 23% of those with hyponatremia and 22% of those with hypocalcemia.

Any electrolyte abnormality which is resistant to supplementation needs magnesium evaluation.[58]

Pre-eclampsia

Magnesium is the agent of choice in the prevention and treatment of eclamptic seizures. The primary objective of magnesium sulphate prophylaxis in women with pre eclampsia is

to prevent or reduce the rate of eclampsia and complication associated with eclampsia.[62]

Magnesium sulphate is effective in preventing and treating eclampsia.[63] Magnesium sulphate halves the risk of eclampsia and probably reduces the risk of maternal death. There do not appear to be substantive harmful effect to mother or baby in the short term.[64]

Magnesuim sulfate has dual action. It interferes with transmission at the neuromuscular junction and also affects the central nervous system. Magnesium sulfate has central anti convulsant activity in animal model, inhibiting the N-methyl-D-aspartate receptor in the brain.[65]

CALCIUM

Calcium is the fifth most abundant element on earth and is the most abundant mineral in the body. It is the principal extracellular divalent cation in the human body. It makes up about 1.5 to 2% of the body weight. Ninety-nine percent of calcium is in the bones and teeth. The remaining 1% is in the blood and extracellular fluids.

Serum Calcium

Normal serum calcium levels ranges from 9.0 - 10.5 mg/dl (2.2 - 2.6 mmol/L). Three forms of calcium are in equilibrium in serum. Diffusible ionised calcium which account for approximately half of total serum calcium, non-diffusible calcium bound primarily to albumin accounts for 45% and diffusible complexes of calcium in the lactate, bicarbonate, phosphate, sulfate, citrate and other anions form the remaining 5%. Ionised calcium is the physiological active form.

The normal serum calcium is maintained by the integrated actions of parathyroid hormone (PTH),[66] vitamin D metabolites, calcitonin, and cytokines such as transforming growth factor β and interluekin-6.

A decrease in serum albumin of 1g/dl results in a decrease of about 0.8mg/dl in total serum calcium. The equilibrium among the three forms of serum calcium is affected by changes in blood pH. Thus at pH 6.8 (acidosis), about 54% of serum calcium is in the ionized form, whereas at pH 7.8 (alkalosis), only 38% is ionized.

Calcium is absorbed mainly in deodenum where an acid medium prevails. Absorption is reduced in alkaline medium. Usually 20 - 30% of ingested calcium is absorbed.

Calcium is excreted in feces, urine and sweat, 130 mg / day calcium is excreted through feces and 2 - 4 mg/kg/day via urine and 15mg /day of calcium is excreted via sweat.

Fetal calcium correlate with intake. Although high urinary excretion has been reported to accompany high-protein diet. The presence of phosphorus decrease calcium excretion.

Caffeine and theophylline intakes are also related to calcium excretion. Consumption of a low calcium diet plus two to three servings of brewed coffee resulted in a greater bone loss from the spine and total body calcium in healthy post menopausal women. (Harris and Dawson - Hughes, 1994). While caffeine consumption has been linked to increased risk of hip fracture in women (Kiel et

al., 1990). Recent studies suggest that drinking one 8 oz glass of milk may offset the risk.

Calcium and Pregnancy

Because of substantive fetal needs 300mg/day and as well as increased renal calcium loss from augmented glomerular filtration, PTH levels were assumed to be increased in pregnant women. However Seeley and co-workers (1997)[67] reported a significant decrease in intact parathormone level during pregnancy. At the same time, they showed a two fold increase in serum concentration of 1,25 dihydroxy vitamin D, which is probably of placental and decidual origin. It increases gastrointestinal absorption to meet the needs of pregnancy.

Total serum calcium levels decline to parallel the decreased serum albumin concentrations (Power and associates 1999). Importantly however, ionised calcium levels are unchanged in pregnancy women (Dahlman and Colleagues, 1994).[68]

Pregnancy – Associated Osteoporosis

It is unlikely that normal pregnancy causes osteopenia in most women (Kaur and associates, 2003).[69] Some women develop idiopathic osteoporosis while pregnant or lactating. The cause of

this is controversial, but most authorities believe that pregnancy unmask preexisting bone disease[70] (Black and co-workers, 2000, Henderson and Colleagues, 2000).[71]

Idiopathic osteonecrosis of the femoral head during normal pregnancy has been described (Chang and associates, 1993;[72] Gribble and Berres, 2001).[73] Most clinician recommend calcium and vitamin D supplementation. Although bone density improves in these women, as well as their offspring, many have chronic osteopenia (Blanch and Co-workers, 1994; Carbone and colleagues, 1995).[74, 75]

Hypertension

Evidence supporting an inverse relationship between calcium intake and blood pressure has strengthened in the past decade. Both children and elderly women appear to benefit from increased calcium take (Gilman et al., 1992; Simon et al., 1992). Low calcium intake is not the only factor contributing to hypertension, but it does play a role.

The role of calcium in gestational hypertension is still not clear. Calcium supplementation has been reported to reduce pregnancy-induced hypertension (Repke and Villar, 1990) and to

have no effect in high risk population. However, supplementation did reduce the incidence of preterm delivery and low birth weight infants.

The role of calcium to prevent pre-eclampsia is as follows. High dose calcium exert a negative feedback effect on parathyroid hormone → lowering of intracellular calcium ion levels → smooth muscle relaxation and diminished responsiveness to pressor stimuli.

Further more calcium supplementation is associated with higher levels of calcium excretion which is coupled with an ion exchange with magnesium resulting in increased levels of serum magnesium → smooth muscle relaxation in blood vessels → control of hypertension (Belzian et al., 1988).

AIM OF THE STUDY

To evaluate serum magnesium and calcium in the prediction of preeclampsia in at risk mothers.

MATERIALS AND METHODS

Study Design : Prospective case control study

Study place : This study was conducted in the department of obstetrics at The Institute of Social Obstetrics and Government Kasturba Gandhi Hospital, Madras Medical College, Chennai.

Study period : October 2006 to September 2007.

Study Population :

Inclusion Criteria

1. Pregnant women of age 18 years and above
2. Singleton pregnancy
3. Gestational age 28-30 weeks
4. Roll over test positive
5. Regular for follow up and compliant
6. Planning to have the delivery in the same institution

Exclusion Criteria

1. Previous preeclampsia.
2. Pregnant women with medical diseases complicating pregnancy like hypertension, diabetes, cardiac, renal, liver disorders, CCF.
3. Known eplieptic patients
4. Multiple pregnancies
5. Pregnant women on drugs like calcium channel blocker, diuretics, drugs containing calcium and magnesium.

Study population:

600 pregnant women with normal blood pressure at the time of recruitment were subjected to roll over test and those who were positive for Roll over Test (288) were selected as study population.

All these women were subjected to serum magnesium and calcium assay. Those who had low levels of serum calcium and magnesium formed the study group (95). The remaining 193 who had normal serum magnesium and calcium levels were taken as controls.

STUDY MANOEUVRE

Pregnant women attending our antenatal outpatient department with normal blood pressure were selected. Detailed history and physical examination including blood pressure and urine for protein and other baseline investigations were done. Pregnant women with normal blood pressure fulfilling our study criteria were selected. They were subjected to roll over test.

Blood pressure measurement:

To ensure accurate reading, an appropriate size blood pressure cuff was used (i.e. 12 x 23cm for normal arm size, for arm size > 35cm cuff size 15 x 33cm), measured after a rest period of 10 minutes, in sitting posture with arm at the level of the heart, [30,76] with phase V Korotkoff sound for diastolic blood pressure.

Roll Over Test:

A test in which a woman lies on her left side for 15 minutes after which blood pressure is recorded. She then rolls into the supine position and after 5 minutes, blood pressure is measured again. A rise in diastolic blood pressure in the supine position of more than 20mm Hg is defined as positive roll over test.[77]

Those pregnant women with positive roll over test were selected as study population. For this study population detailed history, physical examination and baseline investigations were done and recorded in a predesigned proforma.

Heparinised venous blood of 5ml was collected from all pregnant women in the study population and analysed for total serum magnesium and calcium.

All the study population were followed up till delivery. On each follow-up detailed clinical examination including blood pressure and urine for protein were done.

Serum total magnesium concentrations were determined by photometric test using xylidyl blue. Magnesium ions form a purple coloured complex with xylidyl blue in alkaline solution. In the presence of glycolether diamine tetracetic acid, which complexes calcium ions, the reaction is specific. The intensity of the purple colour is proportional to the magnesium concentration.

Serum total calcium concentration was determined by colorimetric test using Arsenazo - III. Calcium with Arsenazo III at neutral pH, yield a blue colored complex. The intensity of the colour formed is proportional to the calcium concentration in the sample.

STATISTICAL ANALYSIS

Data has been entered in excel and analysed using SPSS PC+ and EPI Info 2000 statistical software.

The results were analysed by using T test.

OBSERVATIONS

This prospective study was carried out at the Institute of social obstetrics and Govt. Kasturba Gandhi Hospital during the period of October 2006 to September 2007. 600 pregnant women attending our outpatient department were primarily screened for predilection for PIH based on roll over test. 288 pregnant women with positive roll over test were included in the study.

TABLE - 1

SCREENING WITH ROLL OVER TEST

S.No	Roll Over Test	Number of pregnant women
	Total number of Roll Over Test	**600**
1.	Roll over test positive	288
2.	Roll over test negative	312

Of the 600 women who were subjected to roll over test, 288 women were roll over test positive and remaining were roll over test negative. Roll over test positive women were included in the study population. For all the women with roll over test positive, serum magnesium and calcium levels were measured.

TABLE - 2

STUDY POPULATION

S. No.	Category	No. of Pregnant Women	%
1.	Study group	95	33%
2.	Control group	193	67%

Among the 288 pregnant women with positive roll over test, those who had lower levels of serum Magnesium and Calcium developed preeclampsia were designated as study group (95) and those with normal levels of serum Magnesium and Calcium remained normotensive were designated as control group (193).

Since our study was conducted in the hospital which caters to low socio economic status population and also our institute being tertiary centre, more cases of preeclampsia were seen.

TABLE - 3

AGE DISTRIBUTION

S. No.	Age (yrs)	Control Group n (%)	Study Group n (%)
1.	≤ 20 yrs	9 (4.6%)	14 (14.8%)
2.	21 - 25 yrs	128 (66.3%)	57 (60%)
3.	26 - 30 yrs	44 (22.7%)	12 (12.6%)
4.	≥ 31 yrs	12 (6.4%)	12 (12.6%)

Among the control group most of the cases were in the age group 21-25 years followed by 26-30 years and remaining were more than 31 years.

Among the study group 14.8% were of age less than 20 years and 12.6% were more than 31 years. This observation shows that either end of reproductive age are more susceptible of preeclampsia. Youngest in this study was 19 years and eldest was 37 years. Most of the cases were in the age group 21 - 25 years.

TABLE - 4

PARITY DISTRIBUTION

S. No.	Parity	Control Group n (%)	Study Group n (%)
1.	Primi	126 (65.2%)	72 (75.7%)
2.	G_2	34 (17.6%)	20 (21.1%)
3.	G_3	25 (12.9%)	3 (3.2%)
4.	G_4	8 (4.3%)	0

Among the control group 65.2% were Primi, 17.6% were 2nd gravida, 12.9% 3rd gravida and 4.3% were 4th gravida.

Among the study group 75.7% were primi. This is in conformity with the general incidence of preeclampsia. 21.1% were 2nd gravida, and remaining were 3rd gravida.

TABLE - 5

BOOKING STATUS

S.No.	Booking Status	Control Group n (%)	Study Group n (%)
1.	Booked at Institute of Social Obstetrics & KGH	184(95.3%)	91(95.7%)
2.	Booked elsewhere	9(4.7%)	4(4.3%)
3.	Unbooked	-	-

95.3% in the control group and 95.7% in the study group were booked at the Institute of social obstetrics and Govt. Kasturba Gandhi hospital and remaining were booked elsewhere and attended our out patient department. There were no unbooked cases.

TABLE - 6

SOCIO ECONOMIC STATUS[78]

S. No.	Socio economic status	Control Group n (%)	Study Group n (%)
1.	Class I	-	-
2.	Class II	-	-
3.	Class III	-	-
4.	Class IV	8(4.2%)	3(3.2%)
5.	Class V	185(95.8%)	92(97.8%)

Among the control group 95.8% were in class V socio economic status, 4.2% were belonging to class IV socioeconomic status.

Among the study group 97.8% were belonging to class V socioeconomic status and 3.2% were from class IV socio economic status. This is in expected lines since our hospital essentially caters to population who were below poverty line.

TABLE - 7

BLOOD PRESSURE DISTRIBUTION

S.No.	Blood Pressure (mm Hg)	No. of pregnant women	%
1.	Systolic 100 - 128 Diastolic 70 - 88	193	67%
2.	Systolic 130 -158 Diastolic 90 - 108	61	21%
3.	Systolic $\geq$ 160 Diastolic $\geq$ 110	34	12%

Of the 288 pregnant women who were roll over test positive, during the course of pregnancy 67% remained normotensive with systolic BP in the range of 100 - 128 mm Hg, Diastolic BP 70 - 88 mm Hg, 21% developed mild pregnancy induced Hypertension with systolic BP in the range of 130 - 158 mm Hg and diastolic BP 90 - 108 mm Hg.

12% developed severe pregnancy induced hypertension with the Bp range $\geq$ 160 / 110 mm Hg.

TABLE - 8

DEGREE OF PROTEINURIA

S.No.	Degree of Proteinuria	No. of Pregnant women	%
1.	1+	55	19%
2.	2+	23	8%
3.	≥ 3+	17	6%

19% of the pregnant women were with dipstick proteinuria 1+, 8% with 2+ proteinuria and 6% were with proteinuria ≥ 3+.

TABLE - 9

GA AT WHICH PRE ECLAMPSIA DEVELOPED

S. No.	GA at which preeclampsia developed	No. of pregnant women	%
1.	32-34 wks	61	64.2%
2.	35-37 wks	31	32.6%
3.	≥ 38wks	3	3.2%

During follow up 64.2% developed preeclampsia at 32-34 wks, 32.6% at 35-37 wks and 3.2% developed preeclampsia after 38 wks.

TABLE - 10

MODE OF TREATMENT

S.No.	Treatment	No. of Pregnant women	%
1.	AHT alone	41	43.2%
2.	AHT and MgSo4	9	9.5%
3.	No Treatment	45	47.3%

Of the patients who developed preeclampsia, 41 were treated with Anti hypertensives (AHT) according to our hospital protocol and 9 patient required magnesium sulphate either as prophylactic or therapeutic purpose, remaining were managed expectantly.

TABLE - 11

MATERNAL COMPLICATIONS

S.No.	Maternal Complication	No. of pregnant women	%
1.	Abruption	7	7%
2.	Eclampsia	1	1%
3.	Hellp Syndrome	0	0

Among the patients who developed severe preeclampsia 7 had Abruption, 1 had Eclampsia. No other complications were noted. Since we diagnosed preeclampsia earlier and treated accordingly, the complications were less.

TABLE - 12

MODE OF DELIVERY

S.No.	Mode of Delivery	Control group n (%)	Study group n (%)
1.	Labour Natural	125 (64.7%)	66 (69.4%)
2.	LSCS.	49 (25.3%)	27 (28.4%)
3.	IVD	19 (10%)	2 (2.2%)

Among the control group 64.7% were delivered via naturalis,25.3 by Lower Segment Caesarean Section (LSCS) and the remaining by Instrumental Vaginal Delivery (IVD).

Among the study group 69.4% were delivered via naturalis, 28.4% by Lower Segment Caesarean Section (LSCS) and remaining by Instrumental Vaginal Delivery (IVD).

TABLE - 13

DISTRIBUTION OF BIRTH WEIGHT

S.No.	Birth Weight (kg)	Control Group n (%)	Study Group n (%)
1.	≤ 2	8 (4.1%)	7 (7.5%)
2.	2-2.5	20 (10.4%)	15 (15.7%)
3.	> 2.5	165 (85.5%)	73 (76.8%)

Among the control group 4.1% of babies were less than 2 kg, 10.4% were of weight 2 - 2.5kg and remaining babies were of weight more than 2.5kg.

Among the study group 7.5% of babies were less than 2 kg, 15.7% were of weight 2 - 2.5 kg and 76.8% were more than 2.5 kg weight.

TABLE- 14

FETAL COMPLICATIONS

S.No.	Fetal Complications	Control Group n(%)	Study Group n(%)
1.	IUGR	4 (2%)	4 (4.2%)
2.	Preterm	6 (3.1%)	7 (7.3%)
3.	Respiratory Distress	8 (4.1%)	7 (7.3%)
4.	IUD	-	-

Among the control group 2% has Intra Uterine Growth Retardation (IUGR) babies 3.1% has preterm delivery and 4.1% had respiratory distress.

Among the study group 4.2% had Intra Uterine Growth Retardation (IUGR) babies, 7.3% had preterm delivery and 7.3 babies had Respiratory distress. There was no Intra Uterine death noted.

TABLE - 15

MEAN SERUM MAGNESIUM AND CALCIUM LEVELS

S.No	Category	Number of cases	Serum magnesium (mg/dl)	Serum Calcium (mg/dl)
1	Control Group	193	2.27 ± 0.12	11.02 ± 0.45
2	Study Group	95	1.43 ± 0.10	8.62 ± 0.30

Normal Serum Magnesium is 1.8 - 3 mg / dl. Normal Serum Calcium 9 - 11 mg / dl.

The mean serum magnesium level in the control group was 2.27 ± 0.12 mg / dl and mean serum calcium level was 11.02 ± 0.45 mg / dl. Those who had normal level remained normotensive in the follow up.

The mean serum magnesium level in the study group was 1.43 ± 0.10 mg /dl and mean serum calcium level was 8.62 ± 0.30 mg / dl. Those who had low levels developed preeclampsia in the follow up.

TABLE - 16

COMPARISON OF SERUM MAGNESIUM LEVELS IN CONTROL AND STUDY GROUP

S.No	Category	Number of cases	Serum Magnesium mean ± S.D (mg/dl)	Unpaired T test T value	P value
1	Control Group	193	2.27 ± 0.12	58.59	<0.001
2	Study Group	95	1.43 ± 0.10		

The mean serum magnesium level in the study group who developed preeclampsia were lower than the control group who remained normotensive (1.43 ± 0.10 mg/dl Vs 2.27 ± 0.12 mg/dl, P <0.001), which is statistically significant.

TABLE - 17

COMPARISON OF SERUM CALCIUM LEVELS IN

CONTROL AND STUDY GROUP

S.No	Category	Number of cases	Serum Calcium mean ± S.D (mg/dl)	Unpaired T test T value	P value
1	Control Group	193	11.02 ± 0.45	52.95	<0.001
2	Study Group	95	8.62 ± 0.3		

The mean serum calcium level in the study group who developed preeclampsia were lower than the control group who remained normotensive (8.62 ± 0.30 mg/dl Vs 11.02 ± 0.45 mg/dl, P <0.001), which is statistically significant.

DISCUSSION

This prospective study was carried out at the Institute of Social Obsterics and Government Kasturba Gandhi Hospital in 600 pregnant women attending our outpatient department. All were subjected to roll over test. 288 women were roll over test positive.

Table 1,2 : Serum Magnesium and calcium levels were analysed in these 288 women with positive roll over test. Of these 95 who had low levels of serum Magnesium and Calcium levels were designated as study group and those who had normal levels of serum Magnesium and calcium were designated as control group. 95 of those with low levels of serum Magnesium and calcium developed preeclampsia during the course of pregnancy and 193 of those with normal levels of serum Magnesium and calcium remained normotensive during the course of pregnancy.

Table 3 : Most of the patients who developed preeclampsia were in the age group less than 25 years (74.8%). This is in conformity with the general incidence where preeclampsia is more common in the younger age group.

According to Hauch and Lehmann 1934, preeclampsia is more common in the younger age group(65%)[79].

Table 4 : Most of the patients in the study group who developed preeclampsia were primigravida (75.7%).

This is in conformity with other studies like that of Mac gillivray which showed 15 times higher incidence in primi (Mac gillivray 1959)[80].

Similarly Trupin et al also concluded primi to be at risk for preeclampsia than multipara (Trupin et al, 1996).

Similarly Templeton and Campbell 1979, concluded primi with higher incidence of preeclampsia(65-75%).[79]

Hauth JC, Ewell MG et al., also concluded primi to have higher incidence of preeclampsia(7%).[79]

Table 5 : 95.7% of the patients were booked at the Institute of Social Obstetrics and Government KGH, 4.3% were booked elsewhere. There were no unbooked cases. This may be due to increasing health awareness in the population and governments' effort in maternal and child health and partly may be due to the study conducted at the tertiary level.

Table 6 : 97.8% of the patients were belonging to Class V socioeconomic status. It is because our Institute largely caters to

population below poverty line. According to Duffus and Mac Gillivray 1968, preeclampsia is common in poor socioeconomic class.[79]

Table 7 : In our study during follow up, 67% remained normotensive, nonproteinuric, 21% developed mild preeclampsia and 12% developed severe preeclampsia.

Table 8 : 19% of the patient were with 1+ dipstick proteinuria, 8% with 2+ and 6% with proteinuria > 3+. Chesley 1985 concluded that diagnosis of Preeclampsia is questionable in the absence of proteinuria.[41] Mc Cartney and co-workers (1971) invariable found proteinuria in patients with preeclampsia.[81]

Table 9, 10 : During follow up 64.2% developed preeclampsia at 32-34 weeks, 32.6% at 35-37 weeks and 3.2% developed preeclampsia after 38 weeks. 41 of those who developed preeclampsia were treated with anti- hypertensive treatment alone.

Objective of anti-hypertensive treatment is to prevent intracranial Haemorrhage and left ventricular failure. (Donaldson JO : Neurology of pregnancy, WB saunders Co, 1987).

9 patients in the study group were treated with Magnesium sulphate. Magnesium sulphate is the ideal anticonvulsant in preeclampsia (sibai BM et al 1990).

Pritchard et al 1975 and Zuspan FP et al 1965 observed a better maternal and fetal outcome in severe preeclampsia patients treated with Magnesium sulphate.

According to Altman D, Carroli G et al, 2007[64] use of Magnesium sulphate do not appear to have substantive harmful effects to mother and baby in the short term.

The success of magnesium therapy as a treatment for eclamptic seizures and the known effect of magnesium on vascular response invitro suggested that magnesium might be deficient in women with preeclampsia. This hypothesis was supported by the observation of reduced Magnesium concentration in serum. (James M.Roberts, Judith C Balk et al 2003)[2]

Table 11 : In our study, of those patients who developed severe preeclampsia, 7% had Abruption, 1% had Eclampsia.

In a retrospective study by Al Mulhim AA et al, placental abruption was more common (12.6%) followed by Oliguria (7.9%) and renal failure (4.1%).

In a study by Sibai et al.,[80] placental abruption was more common(20%), followed by HELLP syndrome (5%).

In a study by Friedman SA et al.,[80] of those with severe preeclampsia (5%) had placental abruption and (9%) had Eclampsia.

Table 12 : In the normotensive group 64.7% delivered via naturalis and remaining by Lower Segment Caesarean Section (LSCS) and Instrumental Vaginal Delivery (IVD). Among the preeclamptic group 69.4% had labour natural, 28.4% by caesarean section and 2.2% by Instrumental delivery.

In a study by AL Mulhim AA et al 68.4% had vaginal delivery, remaining had Instrumental Vaginal Delivery (IVD) and Caesarean Section.

Similar results were observed by Cunningham et al,1993.[82]

Table 13,14 : 23% of the babies were of birth weight less than 2.5 kg; of these 4% were IUGR babies and 7% were preterm. Access

to the prenatal care, early detection of preeclampsia, careful monitoring and appropriate management are crucial element in the prevention of preeclampsia related morbidity and mortality.

Various literature emphasizes increased risk of adverse neonatal outcome in the presence of proteinuria and hypertension.

In an analysis by Buchbinder A et al found that preeclamptic women had higher rates of preterm delivery and small for gestational age.

In a retrospective study by Al Mulhim AA et al, perinatal outcome in preeclamptic women showed higher still birth rate (2.34%) and early neonatal death (1.02%).

In our study since we diagnosed preeclampsia earlier and treated accordingly, the neonatal morbidity is less and neonatal mortality is nil.

Table 15, 16, 17 : In our study women who developed preeclampsia had lower levels of serum Magnesium and calcium when compared to women who remained normotensive who had normal levels of serum magnesium and calcium.

The mean serum magnesium levels in the study group who subsequently developed preeclampsia was 1.43 ± 0.10 mg/dl. The mean serum magnesium levels who remained normotensive (control group) was 2.27 ±0.12 mg /dl.

The mean serum calcium levels in the women who subsequently developed preeclampsia (study group) was 8.62 ± 0.30 mg/dl. The mean serum calcium levels in the women who remained normotensive (control group) was 11.02 ± 0.45 mg /dl.

Similar results were observed in the following studies :

According to S.R. Ambwani, UH Shah et al.,[15] the serum magnesium and calcium levels were lower in women with preeclampsia when compared to normotensive pregnant women. Serum magnesium levels were (1.34 ± 0.06 meq/l vs 2.06 ± 0.67 meq/l, P<0.001) serum calcium levels were (7.76 ± 0.37mg / dl vs 9.24 ± 0.15 mg/dl, P<0.01).

According to Sukonpan K, Phupong V study[16], the serum magnesium levels were lower in women with Preeclampsia than normotensive pregnant women (0.77 ± 0.08 mmol/l vs 0.85 ± 0.09 mmol/l, P = 0.001). Serum calcium levels were lower in women

with Preeclampsia compared to normotensive pregnant women (9.0 ± 0.4 mg/dl vs 9.7 ± 0.7 mg/dl, P < 0.0001).

According to Kisters K, Niecher W [83], the serum magnesium levels were lower in Preeclamptic women when compared to normotensive pregnant women (1.31 ± 0.16 mg / dl vs 1.83 ± 0.29 mg / dl, P < 0.001).

In a study by J Kar, R.Jina [84] the serum magnesium levels were found to be lower in women with Preeclampsia compared to pregnant women who remained normotensive (1.51 ± 0.21 mg/dl vs 2.12 ± 0.19 mg/dl, P < 0.001).

In the study by Malas NO, Shurideh ZM[26] also the serum calcium levels in women with Preeclampsia were lower compared to normal pregnant women (8.22 ± 0.12 mg% vs 9.50 ± 0.16 mg%, P < 0.005).

According to Kosch M, Hausberg M et al.,[28] the serum calcium levels in women with Preeclampsia were lower than the levels in normal pregnant women (1.96 ± 0.15 mmol/l vs 2.20 ± 0.10 mmol / l, P < 0.01).

Lower serum magnesium and calcium levels is statistically significant in predicting the Preeclampsia in at risk mothers.

SUMMARY

This prospective study "Evaluation of Serum Magnesium and Calcium in the prediction of Preeclampsia in at risk mothers "was carried out at the Institute of Social Obstetrics and Government Kasturba Gandhi Hospital for women and children , Chennai during the period October 2006 to September 2007.

Observations of this study includes:

- Most of the patients in the study group were in the age group 21-25 years.
- 75.7% of the patients were primigravida.
- 95.7% of the cases were booked at the Institute of Social Obstetrics and Govt Kasturba Gandhi Hospital.
- 97.8% belong to class V socio economic status.
- 21% developed mild preeclampsia and 12% developed severe preeclampsia.
- Of those who developed preeclampsia 64.2% developed preeclampsia at 32-34 weeks of gestation, 32.6% developed preeclampsia at 35-37 weeks and 3.2% developed preeclampsia after 38 weeks.

- Of those who developed preeclampsia, 41 were treated with Antihypertensives alone and 9 were treated with magnesium sulphate.

- Of the 12% who developed severe preeclampsia 7 had Abruption and 1 had Eclampsia.

- 69.4% were delivered via Naturalis, 28.4% by caesarean section and 2.2% by Instrumental vaginal delivery.

- The mean serum magnesium levels in the study group who subsequently developed preeclampsia was 1.43 ± 0.10 mg/dl. The mean serum magnesium levels who remained normotensive (control group) was 2.27 ±0.12 mg /dl.

- The mean serum calcium levels in the women who subsequently developed preeclampsia (study group) was 8.62 ± 0.30 mg/dl. The mean serum calcium levels in the women who remained normotensive (control group) was 11.02 ± 0.45 mg /dl.

- Lower Serum Magnesium and Calcium levels are statistically significant in predicting Preeclampsia for at risk mothers.

CONCLUSION

- Preeclampsia is a multisystem disorder unique to pregnancy.
- Any method which can reasonably indicate the possibility of developing Preeclampsia will be most welcome.
- One such method developed is the measurement of serum magnesium and serum calcium estimation.
- This study conducted at The Institute of Social Obstetrics and Govt. Kasturba Gandhi Hospital reveals estimation of serum calcium and magnesium levels to be a useful indicator for the prediction of preeclampsia.
- This low cost technique is ideally suited as a screening test for women even in resource poor settings like India.

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PROFORMA

Serial No.

O.P. No/IP No.

Unit

Name Age Address Socio Economic status

Booked / Booked outside / Unbooked : Marital status : Unmarried/Married

Immunized : Yes/No

Obstetric History : Gravida Para Live Abortion

LMP :

EDD :

Personal History : Diet, Smoking

H/o Diabetes mellitus, hypertension , renal disease, cardiac disease, liver disease, congestive cardiac failure, epilepsy.

H/o Preeclampsia in the previous pregnancies

Family History : H/o preeclampsia in the mother, sisters

H/o diabetes, hypertension

Drug History : H/o taking any calcium channel blockers, diuretics, drugs containing magnesium and calcium.

Symptoms : Duration of pedal edema, facial puffiness

H/o oliguria, urinary tract infection. Signs and symptoms of imminent eclampsia like headache, giddiness, vomiting, visual disturbances, abdominal pain.

General Examination

Height Weight Anemia

PR

BP

Breast, Thyroid, spine

CVS RS CNS

Per abdomen

Roll over test : Positive / Negative

Investigations

Urine
- Albumin
- Sugar

Hb%

Blood
- Urea
- Sugar
- Creatinine

LFT

Serum total calcium

Serum total magnesium

Follow up BP

USG

Treatment : Anti Hypertensive Treatment (AHT)

Magnesium Sulphate

Mode of Delivery : Labour Natural / Instrumental Vaginal Delivery (IVD) / LSCS

Adverse maternal outcome :

Adverse Fetal outcome :