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Serum Calcium and Magnesium Levels in Women Presenting With Pre- Eclampsia, a Case Control Study in North Coastal Andhra Pradesh

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Abstract:
Background: *Pre-eclampsia is one of the major causes of maternal and fetal morbidity and mortality. The aim of the present study was to find out the relationship of serum levels of calcium and magnesium in mild and severe pre-eclampsia and compared to normal pregnancies. Recent studies indicate that serum levels of calcium and magnesium may have a role in pre-eclampsia.*
Study Design: *The study was done in King George Hospital, Visakhapatnam in North Coastal Andhra, India.*
Materials and Methods: *The blood samples from 50 normal pregnant women taken as controls and 40 cases of mild pre-eclampsia and 10 cases of severe pre-eclampsia were analysed for calcium and magnesium levels.*
Results: *The mean serum calcium concentration in mild pre-eclampsia was 8.66 ± 0.43 mg/dl and in severe pre-eclampsia was 7.84 ± 0.47 mg/dl Vs 9.40± 0.43 mg/dl in controls with a significant p <0.001. The mean serum magnesium concentration in mild pre eclampsia was1.68 ± 0.195 mg/dl and in severe pre-eclampsia was 1.55 ± 0.190 mg/dl Vs 2.10± 0.206 mg/dl in controls with a significant p<0.001.*
Conclusion*: Pre-eclampsia is associated with hypocalcaemia and hypomagnesaemia. Intake of supplements, mainly calcium may help in the reduction of incidence of pre-eclampsia especially in a developing country like India.*
Keywords: *Calcium, Magnesium, Pre-eclampsia.*

I. Introduction

Pre-eclampsia is one of the most common causes of maternal and fetal morbidity and mortality[1]. It is a systemic disease that affects 5 - 7 % of all pregnancies and is the most common disorder of pregnancy. The incidence is about 6% in primigravid women[1]. It is responsible for 15% of premature deliveries[2]. Worldwide preeclampsia is responsible for approximately 14% of maternal deaths[3].

Pregnancy is a phenomenon of maternal adaptation to the increasing demands of growing fetus. This produces impact on the plasma level of some essential ions like magnesium and calcium. Many clinical studies show the relationship between the aggravation of the hypertensive complication and change in the concentration of serum calcium and magnesium in pre-eclamptic mothers.

Preeclampsia is a pregnancy specific syndrome characterized by new onset hypertension and proteinuria occurring usually after 20 weeks' gestation. The National High Blood Pressure Education Program (NHBPEP) Working Group classifies hypertensive diseases in pregnancy into four groups. Chronic hypertension, preeclampsia, preeclampsia superimposed on chronic hypertension and gestational hypertension. Preeclampsia is classified into mild and severe types. Mild Pre-eclampsia was diagnosed in women who had a blood pressure of 140/90mHg or more on two occasions each 6 hours apart associated with proteinuria of at least 300 mg per 24 hours or at least 1+ on dipstick testing. Severe pre-eclampsia was defined as a blood pressure of 160/110 mm Hg or above measured on two occasions each 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. Early detection and prompt management helps in reducing the complications of this condition.

The pathophysiological mechanism is characterized by failure of trophoblastic invasion of the spiral arteries which may be associated with an increased vascular resistance of the uterine artery and a decreased perfusion of the placenta[1].Calcium plays an important role in muscle contraction and regulation of water balance in cells. The active ionized calcium level does not change significantly during pregnancy, although total serum calcium levels decline during pregnancy[4,5,6]. The lowering of serum calcium and increase of intra cellular calcium can cause an elevation of blood pressure in preeclampsia. Low calcium levels in serum results in increased release of parathyroid hormone leading to increase in cytosolic calcium. Increased free intra cellular calcium causes increased vascular smooth muscle reactivity leading to vasoconstriction and rising blood pressure.

Pregnancy courses with hypomagnesemia inversely correlated with gestational age. The hypomagnesemia is associated with hemodilution, renal clearance during pregnancy and consumption of minerals by the growing fetus. High vasopressin levels and albuminuria have been attributed to the cause of lowering of serum magnesium.

II. Materials And Methods

The study population was pregnant women attending the antenatal clinic and admitted in the obstetric ward in King George Hospital, Visakhapatnam. The study consists of 50 cases of normal pregnant women taken as controls and 40 cases of mild preeclampsia and 10 cases of severe preeclampsia. Both controls and cases were both age and socio economically matched.

Inclusion Criteria: All pregnant women are at or beyond 28 weeks of gestation, with singleton pregnancy and in the age group between 15-40 years are included.

Exclusion Criteria: Women with chronic hypertension, renal disease, cardio vascular disease, thyroid disease, liver disease, diabetes mellitus, twin pregnancy and molar pregnancy are excluded.
Blood samples were collected with the consent of the patient and centrifuged and analyzed immediately for serum calcium and magnesium levels.

Estimation Of Serum Calcium: It was done by Orthocresolpthale in complex one method**.**

Principle: At alkaline pH, Calcium binds with Orthocresolphthalein complexone to form a bluish purple complex. The intensity of the color formed is proportional to calcium concentration and is measured at 578 nm. Interference from magnesium is overcome by the presence of 8 hydroxyquinoline in the reagent which binds free magnesium.

Normal serum calcium: 9 -11 mg/dl

Estimation Of Serum Magnesium: It was done by Calmagite method.

Principle: Magnesium ions react in an alkaline medium with the metallochrome dye calmagite to form a chromophore which absorbs at 520 nm. Calcium is excluded from the reaction by complexing with EGTA.

Normal serum Magnesium: 1.8 – 2.4 mg/dl

III. Results

In the present study the mean serum calcium concentration in mild pre eclampsia was 8.66 ± 0.43 mg/dl and in severe pre eclampsia was 7.84 ± 0.47 mg/dl Vs 9.40± 0.43 mg/dl in controls with a statistically significant 'p' value of <0.001. The mean serum magnesium concentration in mild pre- eclampsia was1.68 ± 0.195 mg/dl and in severe pre- eclampsia was 1.55 ± 0.190 mg/dl Vs 2.10± 0.206 mg/dl in controls with a statistically significant 'p' value <0.001.

IV. Discussion

In the present study forty [40] cases of mild preeclampsia and ten [10] cases of severe preeclampsia were studied for serum calcium and magnesium levels. Fifty [50] cases of normal pregnant women were taken for comparison. In all cases and controls, serum calcium and magnesium levels are measured by appropriate methods.

The pregnant woman retains 25 to 30 g of calcium to support the developing fetal skeleton. Maternal calcium absorption from the gut increases significantly in the second and third trimesters, and then declines to pre pregnancy levels with lactation and weaning[7]. Maternal urinary calcium excretion is increased throughout pregnancy[4,6,7]. The level of 1,25dihydroxyvitamin D rises dramatically during pregnancy[4,6,8]. Placenta is the source, which possesses 1- α hydroxylase activity and is able to produce 1,25- dihydroxyvitamin D from its precursor 25- hydroxyvitamin D[9]. Intact Parathyroid hormone levels decrease in the first half of pregnancy, reaching a nadir in the second trimester, and then rising thereafter[4,6,7,10]. The paradoxical decrease in Parathyroid hormone during gestation is due to direct inhibition of Parathyroid by high levels of 1,25 dihydroxyvitamin D or increased intestinal absorption of calcium. Total serum calcium levels decline during pregnancy, the reduction reflecting lowered plasma albumin concentration and, in turn, the consequent decrease in the amount bound to protein. The lowering of serum calcium and increase of intra cellular calcium can cause an elevation of blood pressure in preeclampsia. In the present study the mean serum calcium concentration in mild pre eclampsia was

8.66 ± 0.43 mg/dl and in severe pre eclampsia was 7.84 ± 0.47 mg/dl Vs 9.40± 0.43 mg/dl in controls with a statistically significant p <0.001. The values in the present study are in consistent with the study of J. Chaudhuri et al 2003, Seema Jain et al 2008 and Punthumapol et al 2008 with a significant 'p'value of <0.001.

Magnesium has been known as an essential cofactor for many enzyme systems. It plays an important role in neurochemical transmission and peripheral vasodilatation[11]. There may be a causal relationship since magnesium is involved in blood pressure regulation through an intracellular inhibition of Nitric Oxide Synthase in endothelial cells. The extra cellular magnesium concentration influences calcium metabolism of vascular smooth muscle cells by changing the calcium influx through the plasma membrane. Consequent to hypomagnesaemia, serum calcium also falls which further aggravates the neuromuscular irritability and convulsions. Magnesium sulfate has been used as the drug of choice in severe pre-eclampsia and eclampsia treatment. In the present study the mean serum magnesium concentration in mild pre eclampsia was1.68 ± 0.195 mg/dl and in severe pre eclampsia was 1.55 ± 0.190 mg/dl Vs 2.10± 0.206 mg/dl in controls with a statistically significant p value of < 0.001. The values in the present study are consistent with the study of Seema Jain Et al 2008, Vahidrodsari Et al 2008, Bunyamin Et al 2008, Punthumapol Et al 2008, Sukonpan. K Et al 2005 and J.Chaudhuri Et al 2003 with a significant 'p'value of < 0.001.

V. Conclusion

Pre eclampsia is associated with hypocalcaemia and hypomagnesaemia. Hypocalcaemia may have a role in the etiology of pre eclampsia. Hence calcium supplementation is beneficial in lowering blood pressure and reducing incidence of preeclampsia.

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