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# Association of hypomagnesemia in pre-eclampsia and preterm labor

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**Abstract**
Pregnancy poses to be a rebirth to a mother especially when associated with antenatal complications. Gestational complications like preeclampsia and preterm labor are still ridicule even to the modern-day obstetricians. Certain minerals have been found to be deficient in conditions like Anemia, Pre-eclampsia, Congenital anomalies and Pre-term labor. Vastly studied among them are Iron, Zinc, Magnesium, Calcium, Chromium and Selenium. Though many theories and etiologies have been put forth as to their causation, still the exact inciting factor is yet to be determined. If a disease has many theories it can be presumed the definitive etiology is yet to be identified. One among the several causative factors evaluated is Trace mineral deficiency like Magnesium, Zinc and Chromium. This study was conducted to determine the presence of Magnesium deficiency in women with Pre-eclampsia and Pre-term labor. Magnesium level was assessed in known cases of Preeclampsia and Preterm labor and was compared with controls matched by age Body mass index and gestational age. It was found that there was an association of Hypomagnesaemia in both the conditions as compared with normal controls and can be concluded that substitution of Magnesium along with Calcium would help in prevention of these complications and lead to reduced maternal and fetal morbidity and mortality.

**Keywords:** Hypomagnesemia pre-eclampsia, preterm labor

## Introduction

### Review of literature

Magnesium comprises 2.5% of the Earth's crust. It is considered to be the" Iron "of the plant world abundantly present in Chlorophyll – the blood pigment of plants. Magnesium is a crucial element for photosynthesis and oxidative phosphorylation in the plant kingdom. It is a macro mineral and one of the principal cations of soft tissues – the 4$^{th}$ most abundant cation after potassium in the intracellular compartment. It plays a key role as activator of over 300 enzymes essential for human body metabolism. Several diseases like Arteriosclerosis, Myocardial damage, Hypertension, Arrhythmias, Attention deficit syndrome and Chronic fatigue syndrome, pregnancy complications like Pre eclampsia and preterm labor have been proven to be associated with deficiency of Magnesium in the body. (*Peacock JM, Falsom*)

Kruse and associates made their first systemic observations of magnesium deficiency in rats and dogs in early 1930s. The first description of clinical depletion of Magnesium in man was published in JAMA in 1934 by *Herschfield and Haury*. Magnesium sulphate is now successfully used as a medication for management of Preeclampsia to prevent convulsions and also as an effective tocolytic drug. It is also proven as a neuro-protective agent and is used to prevent HIE in the new born when used for cases of early preterm labor.

### Source of magnesium

Rich source of Magnesium are Green Vegetables rich, fruits, grams and nuts and a slightly lower concentration in animal sources like meat, milk and eggs. Milling of cereals leads to loss of Magnesium. The daily recommended allowance of magnesium in diet is around 40-60mg for infants, 80-160mg for children, 270-350mg for men, 280-300mg for women. Pregnancy and lactation has a requirement of around 320-355mg per day.

### Metabolism and distribution of magnesium

The Human body contains 21 gms of Magnesium of which 70% is in the bones in combination with Calcium and Phosphorus, remaining being in the soft tissues. Intra cellular Magnesium

constitutes around 45%, the concentration in the cells approximately being around 1-2 mmol/L (2.4-3 mg/dl). Within the cell, magnesium is compartmentalized, most of it bound to protein and negatively charged molecules, 80% of cytosolic magnesium is bound to ATP. In blood, Magnesium is present in cells and in the plasma. The magnesium content of RBC is 5-7mg/dl and Plasma is 2-4 mg/dl.

The metabolism of Magnesium is similar to Calcium and Phosphorus, following absorption from the gut via a process of active transport it is distributed throughout the cells of the body. The major excretory pathway is the kidneys that play a pivotal role in maintaining magnesium homeostasis. Normally, 3-6% of the filtered load is excreted and 25% of it is re-absorbed in the proximal tubule. Two-third of the dietary magnesium is excreted in the feces (175 mg / day), Urinary excretion being (105mg/day).

**Fundamental role of magnesium in the body**

Magnesium is a key element in various enzymatic activities involving carbohydrate, fat and protein metabolism in the body; it is needed not only for the synthesis of key enzymes but also acts as an activator and catalyst for various enzymatic reactions.

**Magnesium – calcium interaction**

Magnesium is "*Nature's Calcium Channel Blocker"*. They use overlapping transport system in the kidney and compete with each other for reabsorption. Magnesium causes alteration in calcium distribution by changing the flux of Calcium across cell membranes and displaces calcium on its extracellular binding site. Magnesium further inhibits release of calcium from sarcoplasmic reticulum in response to increased influx from extracellular sites and activates the Calcium-ATPase pump and thus decreases the intracellular calcium concentrations.

**Magnesium and smooth muscle and vascular tone**

Magnesium has its effect on three levels of muscle contraction – Excitation, Excitation-Contraction coupling and Contractile apparatus. Extracellular and membrane magnesium affect vascular smooth muscle contractions by modulating calcium uptake, binding and distribution in smooth muscle cells. (*Grobbee)* In the smooth muscle, magnesium bound to calcium sites prevent calcium binding and thus inhibit contraction of smooth muscle. Deficiency of magnesium will potentiate and higher concentrations will inhibit the action of calcium in the smooth muscle. This is the basis for the theory that Magnesium deficiency is a cause for causation of Pre-Eclampsia and Pre-term labor.

**Magnesium and pregnancy**

A healthy newborn contains about 1 gram of Magnesium at birth- most of this is acquired from the mother during the last two trimesters at a rate of 6mg/day (*Reitz*). Normal levels of serum magnesium in Pregnant – 2.1- 4 mg/dl and in Non-pregnant 1.8-3.6mg/dl. Pregnancy leads to a significant decrease in Serum Magnesium levels owing to both hemodilution and due to increased excretion of Magnesium in the Urine. (*Spalting*). Marginal magnesium deficiency at or before conception may become severe with the increasing demands of pregnancy, especially if combined with anorexia and vomiting. Magnesium deficiency occurs following consumption of diet containing less than 0.8MEq/day (*Callaway*) which is common in the Low socioeconomic group due to Malnutrition and inadequate dietary consumption.

Magnesium plays a vital role in smooth muscle contractibility and its deficiency is related to occurrence of Preterm labor as the uterine myometrial and cervical smooth muscle contractility is altered and is more prone for premature onset of uterine contractions and cervical effacement and dilatation. (*Skaja*)

The *US Panel* on "*Study of Nutritional Status in Pregnancy*" estimated an incremental need of 20mg/day to cover both maternal and fetal needs. This was doubled to 40mg/day as there is only 50% absorption of dietary magnesium.

**Pharmalogical uses of magnesium**

Magnesium is therapeutically used as MgSo4.7H2O – 1 gm. of this salt contains 98mg of elemental magnesium. It exerts its effect on both central and peripheral actions. It causes smooth muscle relaxation – useful to treat preterm labor. It inhibits release of Acetylcholine in response to motor nerve impulse. It is a NMDA (*N-Methyl D-Aspartate*) receptor antagonist-useful in preventing convulsions. Mgso4 acts by opposing calcium dependent arterial vasoconstriction, causes vasodilatation and increases cerebral blood flow - this property is utilized in its use in management of severe hypertension and prevention of convulsions.

**Estimation of magnesium levels**

Photometric method and Atomic absorption spectrometry are used in the estimation of serum magnesium levels. Assessment of serum magnesium is commonly done to evaluate its level following Mgso4 administration and if there is suspicion or evidence of toxicity.

| Blood level | Signs and symptoms |
|---|---|
| 4-8 mg/dl | Therapeutic |
| 9-12 mg/dl | Nausea, feeling of warmth, flushing, double vision, slurred speech, weakness and loss of patellar reflex |
| 13-17 mg/dl | Muscular paralysis and respiratory arrest |
| 30-35 mg/dl | Cardiac arrest |

**Aim of study**

The study design is a case control comparative study -the study was conducted to evaluate the level of serum Magnesium in cases of Pre eclampsia and cases of Pre-term labor. Level of Magnesium in Pre – eclampsia patients was compared with women of normal blood pressure and no proteinuria and levels evaluated for pre-term labor was compared with control women who delivered after 37 weeks of gestational age.

**Materials and methods**

A total of 128 women with Mild Preeclampsia and 72 women with Severe Pre eclampsia were studied and compared with a control of 200 normotensive women. A total number of 50 Pre-term labors were selected and levels of serum Magnesium was compared with 50 matched counterparts with none of the complications.

**Study analysis**

**Table 2:** Analysis of Magnesium levels in Pre-eclampsia and controls

| Category | Number (n) | Mean level of Magnesium | P value |
|---|---|---|---|
| Mild Preclampsia | 128 | 1.712 | <0.001 Significant |
| Severe Preeclampsia | 72 | 1.496 | |
| Control | 200 | 2.232 | |

**Table 3:** Analysis of Magnesium levels in Pre -term labor and controls

| Category | Number (n) | Mean value of S. Magnesium | P value |
|---|---|---|---|
| Pre –term labor (28-36+6WEEKS) | 50 | 1.505 | <0.001 Significant |
| Labor after 37 weeks | 50 | 2.308 | |

The values of the study is supporting the findings of various studies done in the previous years that have also proved a lower level of serum Magnesium in Pre –eclampsia and in Pre-term labor was present when compared with women who were normotensive and women who delivered after 37 weeks of gestation.

## Summary and conclusion

The nutritional status of a woman before and during pregnancy determines the successful outcome of a pregnancy. Various trace elements and minerals are essential for the mother and fetus of which magnesium is one of them, this study supports the fact that lowered serum level of Magnesium can adversely affect pregnancy by causing Pre eclampsia and Pre-term labor. The study also emphasizes the fact that Magnesium supplementation in the antenatal period along with Calcium and Iron would be useful in preventing complications like Pre-eclampsia and Pre - term labor.

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