

# A Study Of Serum Calcium, Magnesium & Urine Microalbumin Levels In Normal & Pre-Eclamptic Gestation & To Compare With Non-Gestational Value In A Tertiary Health Care Centre In North-East India

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## Abstract:

**Introduction:** Pre-Eclampsia is a multi-system disorder of unknown aetiology, unique to pregnancy, onset after 20 weeks of gestation with hypertension to the extent of 140/90 mm Hg or more, and proteinuria ( $\geq 300$ mg/day) and edema. FOGSI (The Federation of Obstetric & Gynaecological Societies of India) and other studies show the incidence of Pre-Eclampsia in India ranges between 11-13%. And in North-East region of India it is very much common. NFHS has been conducted in India for three successive rounds. Among states highest prevalence found in Tripura (87.5%) and lowest prevalence state Haryana (33.3%). The cause of Pre-Eclampsia remains unknown and the only known cure is delivery of the fetus and placenta. Despite decades of research into the condition, predicting which women are at increased risk of developing Pre-Eclampsia remains problematic. Identifying "at-risk" women is an important aim. Our aim in the present study was the levels microalbuminuria in predicting hypertensive complications and to determine the changes in the levels of minerals (Calcium & magnesium), if any, as a biochemical marker of pregnancy induced hypertension in normal and Pre-Eclampsia gestation & to compare with non gestational value.

**Materials and methods:** The Study conducted in three broad groups:

**Group A (n=50)** Consist of non-pregnant normotensive women. The age group was 18-35 years (mean age 24 years).

**Group B (n=50)** Consist of women having normal uncomplicated pregnancy without hypertension. The age group was 18-35 years (mean age 22 yrs).

**Group C (n=50)** Consist of women with Pre-Eclampsia. The age group was 18-35 years (mean age 24 yrs).

**Statistical evaluation, Interpretation, comparison and correlation of findings in the groups.**

**Results:** To compare Serum calcium, magnesium levels and urine microalbumin level in Pre-Eclampsia patients as compared to healthy pregnant controls with Non-Pregnant normotensive women. To find out any possible correlation of their levels with the severity of the disease.

**Conclusion:** On the basis of our results we conclude the study that, Hence, it can be concluded that: Statistically significant decrease was seen in serum Calcium and Magnesium in Pre-Eclamptic women as compared to normal pregnant and non-pregnant women. Statistically significant increase was seen in Urine Microalbumin in Pre-Eclamptic women as compared to normal pregnant women, can be used as tool in making decision, regarding the management strategies to improve the maternal and fetal outcome.

**Keywords:** Non-pregnant normotensive women, uncomplicated pregnancy without hypertension, women with Pre-Eclampsia, serum Calcium and Magnesium, urine microalbumin.

## I. INTRODUCTION

Pregnancy is a physiological state associated with many alterations in metabolic, biochemical, physiological, haematological and immunological processes. If there are no

complications, all these changes are reversible following a few days to a few months after delivery.

Hypertensive disorders of pregnancy and their complications rank as one of the major cause of maternal

mortality and morbidity in the world. It accounts for approximately a quarter of all antenatal admissions.

In addition, as it is strongly associated with fetal growth retardation and prematurity, it also contributes largely to perinatal mortality and morbidity.

Pre-Eclampsia is a multi-system disorder of unknown aetiology, unique to pregnancy, onset after 20 weeks of gestation with hypertension to the extent of 140/90 mm Hg or more, and proteinuria ( $\geq 300\text{mg/day}$ ) and edema.

Pre-Eclampsia subdivided into –

**MILD PRE-ECLAMPSIA:** Defined as Pregnant female of  $>20$  weeks of gestation with blood

pressure  $\geq 140/90$  mm of Hg &  $<160/110$  mm of Hg noted first time during pregnancy on  $\geq 2$  occasions at least 6 hours apart with proteinuria of  $\geq 1+$  ( $\geq 30\text{mg/dl}$ ) by dipstick method in a random urine sample would be considered as having mild Pre-Eclampsia after excluding urinary tract infection.

**SEVERE PRE-ECLAMPSIA:** Defined as the presence of 1 of the following symptoms or signs -

- ✓ SBP of 160 mm Hg or higher or DBP of 110 mm Hg or higher on 2 occasions at least 6 hours apart while the patient is in bed rest.
- ✓ Proteinuria of 5gm or higher in a 24-hour urine specimen or 3+ or greater on two random urine samples collected atleast 4 hours apart 3+ on 2 random urine samples collected at least 4 hours apart within 7 days.
- ✓ Oliguria of less than 500ml in 24 hours.
- ✓ Cerebral or visual disturbances.
- ✓ Pulmonary edema.
- ✓ Cyanosis.
- ✓ Epigastric or right upper quadrant pain.
- ✓ Impaired Liver function.
- ✓ Thrombocytopenia (platelets  $<100000$  cells/micro lit of blood).
- ✓ Intrauterine growth restriction.

Without intervention, Pre-Eclampsia progresses to Eclampsia, this is characterized by malignant hypertension and epileptiform convulsions requiring emergency caesarean section.

Pre-Eclampsia complicates 2-8% of pregnancies and is a major cause of maternal morbidity, perinatal mortality & morbidity and premature delivery.

The worldwide incidence of Pre-Eclampsia varies greatly and it ranges between 2% and 10% of pregnancies. WHO estimated the incidence of Pre-Eclampsia to be seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%).

Hypertensive disorders of pregnancy and their complications rank as one of the major cause of maternal mortality and morbidity in the world after obstetric haemorrhage, pre-existing medical disorders, sepsis and abortions. It accounts for approximately a quarter of all antenatal admissions.

FOGSI (The Federation of Obstetric & Gynaecological Societies of India) and other studies show the incidence of Pre-Eclampsia in India ranges between 11-13%. And in North-East region of India it is very much common. India's third National Family Health Survey (NFHS-3 2005-06) collected data from 124385 women residing in 109041 households. The findings for prevalence of Pre-Eclampsia by India's state and

rural/urban residence. More than half of the respondents ( $n = 22061$ ; 55.6%) had reported symptoms of Pre-Eclampsia. Almost similar prevalence for Pre-Eclampsia was found in rural (56.2%) and urban (54%) India though higher rates ( $>70\%$ ) were observed in the states of Uttarakhand, Bihar, Jharkhand, Kerala with the highest being in Tripura (87.5%) and lowest prevalence State (Haryana-33.3%).

Despite decades of research into the condition, predicting which women are at increased risk of developing Pre-Eclampsia remains problematic. Identifying "at-risk" women is an important aim.

Our aim in the present study was the levels microalbuminuria in predicting hypertensive complications and to determine the changes in the levels of minerals (Calcium & magnesium), if any, as a biochemical marker of pregnancy induced hypertension in normal and Pre-Eclampsia gestation & to compare with non gestational value.

## II. AIMS AND OBJECTIVES

- ✓ To compare urine microalbumin levels in normal pregnant women and in women with Pre-Eclampsia & to compare with non gestational value.
- ✓ To compare serum calcium & magnesium levels in normal pregnant woman and in woman with Pre-Eclampsia & to compare with non gestational value.
- ✓ To find out any possible correlation of their levels with the severity of the disease.

## III. SCHEME OF STUDY

- ✓ All Antenatal cases with gestational age  $>20$  weeks between 18yrs and 35yrs of age as per the inclusion and exclusion criteria were admitted under OBG department, GAUHATI MEDICAL COLLEGE & HOSPITAL in a period between May 2015 to April 2016.
- ✓ A total 150 women were studied for serum Calcium, Magnesium & Urine Microalbumin.
- ✓ The Study conducted in three broad groups:
  - Group A ( $n=50$ ) Consist of non-pregnant normotensive women. The age group was 18-35 years (mean age 24 years).
  - Group B ( $n=50$ ) Consist of women having normal uncomplicated pregnancy without hypertension. The age group was 18-35 years (mean age 22 yrs).
  - Group C ( $n=50$ ) Consist of women with Pre -Eclampsia. The age group was 18-35 years (mean age 24 yrs).
- ✓ Statistical evaluation, Interpretation, comparison and correlation of findings in the groups.

## IV. INCLUSION CRITERIA

- Study was conducted in three broad groups:
- Group A ( $n=50$ ) Consist of non-pregnant normotensive women. The age group was 18-35 years (mean age 24 years).
  - Group B ( $n=50$ ) Consist of women having normal uncomplicated pregnancy without hypertension. The age group was 18-35 years (mean age 22yrs).

Group C (n=50) Consist of women with Pre-Eclampsia. The age group was 18-35 years (mean age 24 yrs).

### V. EXCLUSION CRITERIA

Subjects with following condition excluded from the study

- ✓ Pregnant women with essential hypertension or hypertension <20 weeks gestation.
- ✓ Pre-existing diabetes mellitus, renal disease, liver disorder, heart disease, epilepsy & with urinary tract infection.

### VI. MATERIALS AND METHODS

- ✓ All the studies and investigations were carried out after obtaining informed consent from the participating subjects.
- ✓ Quantitative analysis of Fasting Plasma Glucose, kidney function test was measured using standard methods and kits among three study groups.
- ✓ The two groups (B & C groups) were matched according to maternal age (years) and gestational age (weeks) / trimester.
- ✓ Routine Examination (Physical, Chemical, and Microscopy) of Urine (Random Sample) were done among three study groups.
- ✓ Urinary Protein estimation by Heat Coagulation method was done among three study groups.
- ✓ Microalbumin in urine samples were estimated by Accucare kit on Micro-lab 300 semiautomatic auto analyzer among three study groups.
- ✓ Serum level of Calcium & Magnesium were estimated by Micro-lab 300 Semiautomatic auto analyzer by Roche diagnostics among three study groups.
- ✓ Demographic data (age, sex, weight, height, BMI, duration of disease, associated complications) determined by using existing standards, medical records and proper history taking.
- ✓ Evaluation, interpretation, comparison, and correlation of findings in the three groups done by appropriate statistical techniques.
- ✓ All the cases were informed about the study and asked to give written consent to participate in the study.
- ✓ Consent from ethical committee was also taken to carry out the above research.
- ✓ 5 ml of venous blood and urine samples were collected and calcium, magnesium & microalbumin tests were performed.
- ✓ Statistical analysis -
  - All the values were expressed as mean ± SD. One way Analysis of variance (ANOVA) test were used to analyze differences in baseline characteristics between the studied groups.
  - p value <0.05 was considered as statistically significant, that <0.001 was considered as highly significant.

- Pearson's correlation coefficient (r) was calculated to assess the correlation between biochemical parameters and the blood pressure.
- Data was analyzed using Graph Pad Instat version 3.00 software.

### VII. RESULT & OBSERVATION

#### DEMOGRAPHIC & ANTHROPOMETRIC DATA

Mean age, gestational age and body mass index between Non-Pregnant normotensive women (A), Normal Pregnancy (B), Pre-Eclampsia(C).

Parameter	A	B	C
Age (Years)	24.63±3.85*	24.62±2.92*	26.6±4.32*
Gestational Age (Weeks)	24.36±3.135*	32.6±1.99*	38.6±2.18*
BMI (Kg/m <sup>2</sup> )	20.46±3.43*	20.17±3.613*	20.5±3.70**

\* Non significant

\*\* Significant

Table 1

#### VITAL PARAMETERS

The mean systolic, diastolic blood pressures were increased significantly in the Pre-Eclampsia Patients(C) compared to Non-Pregnant normotensive women (A), Normal Pregnancy healthy pregnant (A) controls.

Parameter	A	B	C
Systolic blood pressure (mm Hg)	103.82±11.65	102.72±12.027	173.86±10.770**
Diastolic blood pressure (mm Hg)	79.28±11.78	80.44±11.44	143.08±15.47**

\*\* Significant

Table 2

#### BIOCHEMICAL PARAMETERS

Serum calcium, magnesium levels were decreased statistically and urine microalbumin level increased significantly in Pre-Eclampsia (C) patients as compared to healthy pregnant controls(B) with Non-Pregnant normotensive women(A).

Parameter	A	B	C
Serum Calcium (mg/dl)	9.6±1.0	8.94±0.32**	7.9±0.56***
Serum Magnesium (mg/dl)	2.4±0.6	2.1±0.3**	1.96±0.4***
Urine Micro albumin (mg/dl)	26±6	29±5**	95±34***

\*p <0.01 normal pregnancies as compared to Pre-Eclamptic pregnancies.

\*\*p <0.05 normal pregnancies as compared to Pre-Eclamptic pregnancies.

\*\*\*p <0.001 normal pregnancies as compared to Pre-Eclamptic pregnancies.

Table 3

CALCIUM

The mean ±SD Calcium Values in Group A, B & C are 9.6 ± 1.0, 8.94 ± 0.32, 7.9 ± 0.56(mg/dl) respectively. There was a decreased in serum Calcium values in both Group B and Group C as compared to Group A. But the decreased was statistically significant (p<0.05) in Group C only.

Our study showed that serum total calcium level significantly decreased in Pre-Eclamptic women than in healthy pregnant women.

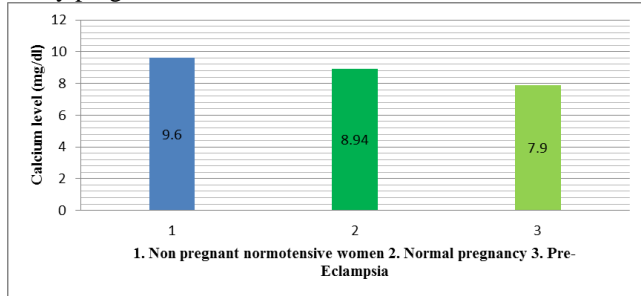


Figure 1

MAGNESIUM

The mean ±SD Magnesium values in Group A, B & C were 2.55±0.26, 2.63±0.30, 1.82±0.12 (mg/dl) respectively. There is a statistically significant decreased in serum Magnesium values in both Group B & Group C as compared to Group A.

Serum total magnesium concentrations were significantly lower in Women with preeclampsia relative to normal pregnant controls.

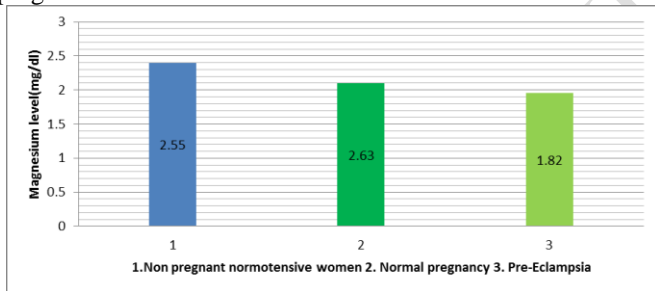


Figure 2

MICROALBUMIN

The mean ±SD Microalbumin values in Group A, B & C are 25.36 ±2.37, 37.18±3.97, 87.18±4.44 (mg/dl) respectively. There is a statistically significant increased in Microalbumin values in Group C as compared to Group A.

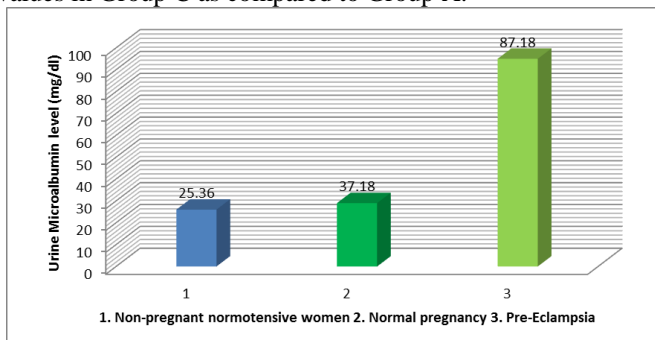


Figure 3

CORRELATION OF SEVERITY

When serum calcium, magnesium and urine microalbumin levels were correlated independantly with systolic and diastolic blood pressure, a significant negative correlation was obtained between serum calcium and magnesium and a significant positive correlation was obtain with urine microalbumin.

Parameter	Systolic Blood Pressure	Diastolic Blood Pressure
Serum calcium	r= -0.9176. p=0.2602	r=-0.9289. p=0.2415
Serum magnesium	r= -0.7357. p=0.4737	r=-0.7553. p=0.4550
Urine microalbumin	r=0.9971. p=0.0488	r=9989. p=0.0301

Where r - Karl Pearson correlation Co-efficient (-1 to +1).  
p<0.05= statistically significant; p<0.001= highly significant.

Table 4

VIII. DISCUSSION

- ✓ Kisters et al. showed significantly decreased serum calcium content in Pre-Eclampsia compared to healthy pregnant women and our finding also agreed with that study. The underlying facts of decreased serum total calcium concentration in Pre-Eclampsia may be an alteration of the plasma protein concentration (primarily albumin but globulin also bind calcium) results in parallel changes in total plasma calcium. This can be attributed to the fact the reduction was attributed to the expanded intravascular space occurring during pregnancy which was reflected by the reduction of serum albumin as Ca bound to serum protein mainly Albumin represents about 30-45% of total Ca. A pregnant woman's body requires 25-30 gm of Ca to support the developing fetal skeleton which may contribute for this reduction. In contrast, other reports showed that maternal serum total Ca does not vary with increased in gestational age. While other reports have shown that there is increase in serum Ca in pregnant women compared to non-pregnant women.
- ✓ The role of Serum Magnesium appears to be associated with its function as an activator of enzymes involved in membrane transport and integrity, and with its relationship to prostaglandins-specifically, the ratio of prostacyclins (vasodilators) and thromboxanes (some of which are vasoconstrictors), which is dramatically altered in the case of low serum magnesium.<sup>19</sup> Both prostacyclin and thromboxane substances are increased during a normal pregnancy. However, women who develop Pre-Eclampsia have much smaller increases in prostacyclin production than other women, while thromboxane continues to rise at the same rate, thus increasing vasoconstriction and raising blood pressure.<sup>20</sup> We also agree with this theory. Therefore, low serum total

magnesium concentration in Pre-Eclampsia may be a factor in the etiology of this disease.

- ✓ Albumin is smaller and therefore more likely to escape through the filters of the kidney, called glomeruli. Albumin's function in the body includes retention of fluid in the blood. It acts like a sponge, soaking up fluid from body tissues. Hypertension may cause renal insufficiency, which may cause proteinuria. In normal pregnancy total protein level in mother is low due to supply to foetus. Serum albumin levels are also decreased.<sup>21</sup> In Pre-Eclampsia group total protein and albumin level but not globulin is lower than uncomplicated pregnancy. It may be due to loss of protein in the urine. Lower protein and albumin level in Pre-Eclampsia subjects was also found by Anne Barden et al.

#### IX. CONCLUSION

- ✓ Hence, it can be concluded that: Statistically significant decrease was seen in serum Calcium and Magnesium in Pre-Eclamptic women as compared to normal pregnant and non-pregnant women.
- ✓ Statistically significant increase was seen in Urine Microalbumin in Pre-Eclamptic women as compared to normal pregnant women.
- ✓ Reduction in serum levels of calcium and magnesium, during pregnancy might be possible contributors in etiology of Pre-Eclampsia, and supplementation of these elements to diet may be of value to prevent Pre-Eclampsia.
- ✓ As proteinuria is one of the classic signs of Pre-Eclampsia, the presence of microalbuminuria in some otherwise symptom-free patient confirms that changes in renal function are present in whom Pre-Eclampsia as will eventually develop. Early pregnancy levels of microalbuminuria can be used as predictors of Pre-Eclampsia with high negative predictive value.

#### REFERENCES

- [1] Maternal physiology. In : Cunningham F, Lenevo K, Bloom S, Hauth J, Gilstrap L, Wenstrom K (eds). Williams Obstetrics, 23rd edn. Mc Graw Hill, New York 2011, pp107-131.
- [2] Cengiz C, Kimya Y. Maternal Fizyoloji. Temel Kadın Hastalıkları ve Dogum Bilgisi (Eds Kisisçi et al) Günes, Ankara.1997; 242-243.
- [3] Chapman JF, Tsongalis GJ. Pregnancy and fetal development. In: Kaplan LA, Pesce AJ, eds. Clinical Chemistry. Missouri: Mosby; 1996:799-810.
- [4] Herrera E, Gomez DC, Lasuncion MA. Lipid metabolism in pregnancy. Biol Neonate. 1987; 52(2):70-77.
- [5] Park K. Textbook of preventive and social medicine. 21st edn. M/s Banarasidas Bhanot publishers; 2011. Chapter: Preventative medicine in obstetrics, pediatrics & geriatrics: 514-517.
- [6] Cunningham F, Lenevo K, Bloom S, Hauth J, Gilstrap L, Wenstrom K. In Maternal physiology. Williams Obstetrics 23rd edn. New York 2011; Mc Graw Hill: 707.
- [7] Packer CS. Biochemical markers and physiological parameters as indices for identifying patients at risk of developing pre-eclampsia. J Hypertens. 2005; 23(1): 45-46.
- [8] Duley L. Pre-eclampsia and the Hypertensive disorders of pregnancy. Br Med J. 2003; 67: 161.
- [9] WHO. Make every mother and child count. The World Health Report. 2005; Geneva Switzerland: World Health Organization.
- [10] Park K. Textbook of preventive and social medicine 21st edn. Preventative medicine in obstetrics, pediatrics & geriatrics. 2011; M/s Banarasidas Bhanot publishers: 514-517.
- [11] Bansal S. Hypertension in pregnancy. In: Desai P, Malhotra N, Shah D eds. Principles & practice of Obstetrics & Gynaecology for post-graduates. 3rd ed. Jaypee Brothers, New Delhi, 2008; 100-107.
- [12] International Institute for Population Sciences & Macro International: National Family Health Survey (NFHS-3), 2005–06: India: Vol. I. Mumbai, IIPS; 2007.
- [13] Agrawal, Walia. J Womens Health Issues Care. 2014; 3: 6 <http://dx.doi.org/10.4172/23259795.1000169>.
- [14] Kisters K, Barenbrock M, Louwen F, et al. Membrane, intracellular, and plasma magnesium and calcium concentrations in preeclampsia. Am J Hypertens. 2000;13: 765-769.
- [15] Rogers MS, Hedy YM, Fung HY and Hung CY. Calcium and low-dose Aspirin prophylaxis in women at high risk of pregnancy induced hypertension. Hypertens Pregnancy. 1999; 18:165-172.
- [16] Trotter M, Hixon BB. Sequential changes in weight, density, and percentage ash weight of human skeletons from an early fetal period through old age. Anat Rec 1974; 179: 1–18.
- [17] Ardawi MS, Nasrat HA, BA'Aqueel HS. Calcium-regulating hormones and parathyroid hormone-related peptide in normal human pregnancy and postpartum: a longitudinal study. Eur J Endocrinol 1997; 137: 402-409.
- [18] Paderson EB, Johneson P, Kristensen S, Rasmussen AB, Emmertsen K, Moller J, et al. Calcium, Parathyroid hormone and Calcitonin in normal pregnancy and preeclampsia. Gynecol Obstet Invest 1984; 18:156 – 164.
- [19] Zhonghua Fu Chan KeZaZhi.: Magnesium and calcium concentration of peripheral serum and mononuclear cells in patients with pregnancy induced hypertension. 1997 Jan; 32(1):15-8.
- [20] Myatt L, Miodovnik M. Prediction of pre-eclampsia. Semin Perinatol. 1999; 23:45-57.
- [21] Rodriguez MH, Masaki DI, Mestman J, Kumar D, Rude R Calcium/creatinine ratio and microalbuminuria in the prediction of pre-eclampsia. Am J Obstet Gynecol 1988; 159:1452.
- [22] Barden A, Jackie R, Barry W, Constantine M, Jennifer R, Trevor M, Kevin C and Lawrie B. Study of plasma factors associated with neutrophil activation and lipid

peroxidation in preeclampsia. Hypertension. 2001; 38:  
803-804.

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