

# DETERMINATION OF MINERAL, PARATHYROID HORMONE AND 6-KETO-PROSTAGLANDIN-F<sub>1α</sub> LEVELS IN PREGNANT WOMEN WITH HYPERTENSION AND PRE-ECLAMPSIA

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## ABSTRACT

Determinations of total calcium, total magnesium, calcium ion, parathyroid hormone and 6-keto-prostaglandin-F<sub>1α</sub> levels were carried out on 84 blood samples from 4 groups of women categorised as non-pregnant normotensive (NNP), pregnant normotensive (NP), pregnancy-induced hypertension (PIH) and pre-eclampsia (PE). PIH was clinically diagnosed when the diastolic pressure was more than 90 mmHg and was only hypertensive during pregnancy while PE was with additional proteinuria after 20 weeks of gestation. Compared to NNP women, total calcium and parathyroid hormone levels were of lower levels ( $p < 0.05$ ) in NP women while in PIH women, total calcium and 6-keto-prostaglandin-F<sub>1α</sub> levels were also lowered ( $p < 0.05$ ). Compared to NNP women, PE women's levels of total calcium, calcium ion and 6-keto-prostaglandin-F<sub>1α</sub> decreased ( $p < 0.05$ ) while parathyroid hormone level increased ( $p < 0.05$ ). When compared to the NP women, PE women had decreased levels ( $p < 0.05$ ) of total calcium as well as calcium ion and increased level ( $p < 0.05$ ) of parathyroid hormone. Calcium ion was found to be negatively correlated (NNP :  $r = -0.883$ ,  $p = 0.008$  / NP :  $r = -0.931$ ,  $p = 0.000$ ) while parathyroid hormone was positively correlated (NNP :  $r = 0.904$ ,  $p = 0.013$  / NP :  $r = 0.913$ ,  $p = 0.000$ ) with mean arterial pressure.

**Keywords:** calcium, magnesium, parathyroid hormone, 6-keto-prostaglandin-F<sub>1α</sub>, pre-eclampsia

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## INTRODUCTION

Hypertension has always been a major problem to manage in the field of Medicine. It is also widely known as a silent killer which if not detected early may cause death<sup>(1)</sup>. Pregnancy accompanied by hypertension is fatal to both mother and foetus. Various changes occur during pregnancy, which are aggravated with the presence of hypertension. Pregnancy-induced hypertension (PIH) is only detected during pregnancy by signs of a higher blood pressure than normal, without any signs of abnormal proteinuria or edema, and the blood level will decrease to normal within the puerperal period. Pre-eclampsia (PE), on the other hand, is present with similar symptoms as PIH plus significant proteinuria. It has been reported that pre-eclampsia and eclampsia kill about 5 million pregnant mothers and their fetuses annually in the

world<sup>(2)</sup>.

In 1984, Erne and associates<sup>(3)</sup> found an increase in free calcium in platelets of PIH compared to normotensive pregnant women. In 1991, Frolich and coworkers<sup>(4)</sup> found lowered levels of serum parathyroid hormone in PE compared to normotensive pregnant women in the third trimester. In 1992, Seely and coworkers<sup>(5)</sup> reported findings of decreased urinary calcium, increased serum Vitamin D levels in PE compared to normotensive pregnant women. To investigate Malaysian PIH and PE patients, in this study we measured calcium, magnesium, PTH and 6-keto prostaglandin-F<sub>1α</sub> (6-keto-PGCF<sub>1α</sub>), a stable metabolite of prostacyclin. Calcium and 6-keto-PGF<sub>1α</sub> are involved in the regulation of blood pressure while magnesium and PTH are important components of calcium homeostasis.

## MATERIALS AND METHODS

Blood samples from 84 individuals were obtained, of which 18 were non-pregnant normotensive (NNP), 24 were pregnant, normotensive (NP), 26 were women with pregnancy-induced hypertension (PIH) and 16 were women with pre-eclampsia (PE). All subjects were between the ages of 20 and 40 years and pregnant subjects were in their third trimester. PIH subjects were clinically characterised with a diastolic pressure of more than 90 mmHg and were only hypertensive during pregnancy while PE subjects had proteinuria, a protein volume of more than 300 mg/ml urine over 24 hours. The distribution of samples are as illustrated in Table I. Blood samples of 10 ml from each subject were separated into plasma and serum. They were then kept at a temperature of -70°C till further analysis was done.

Serum total calcium and magnesium were measured by atomic absorption spectrophotometry at a wavelength of 422.7 nm and 285.2 nm respectively<sup>(6)</sup>. The measurement of calcium ion levels involved Biuret and Bromocresol Green tests<sup>(7)</sup>. Serum parathyroid hormone levels were measured by a radioimmunoassay kit (Nichols Institute Diagnostic). The

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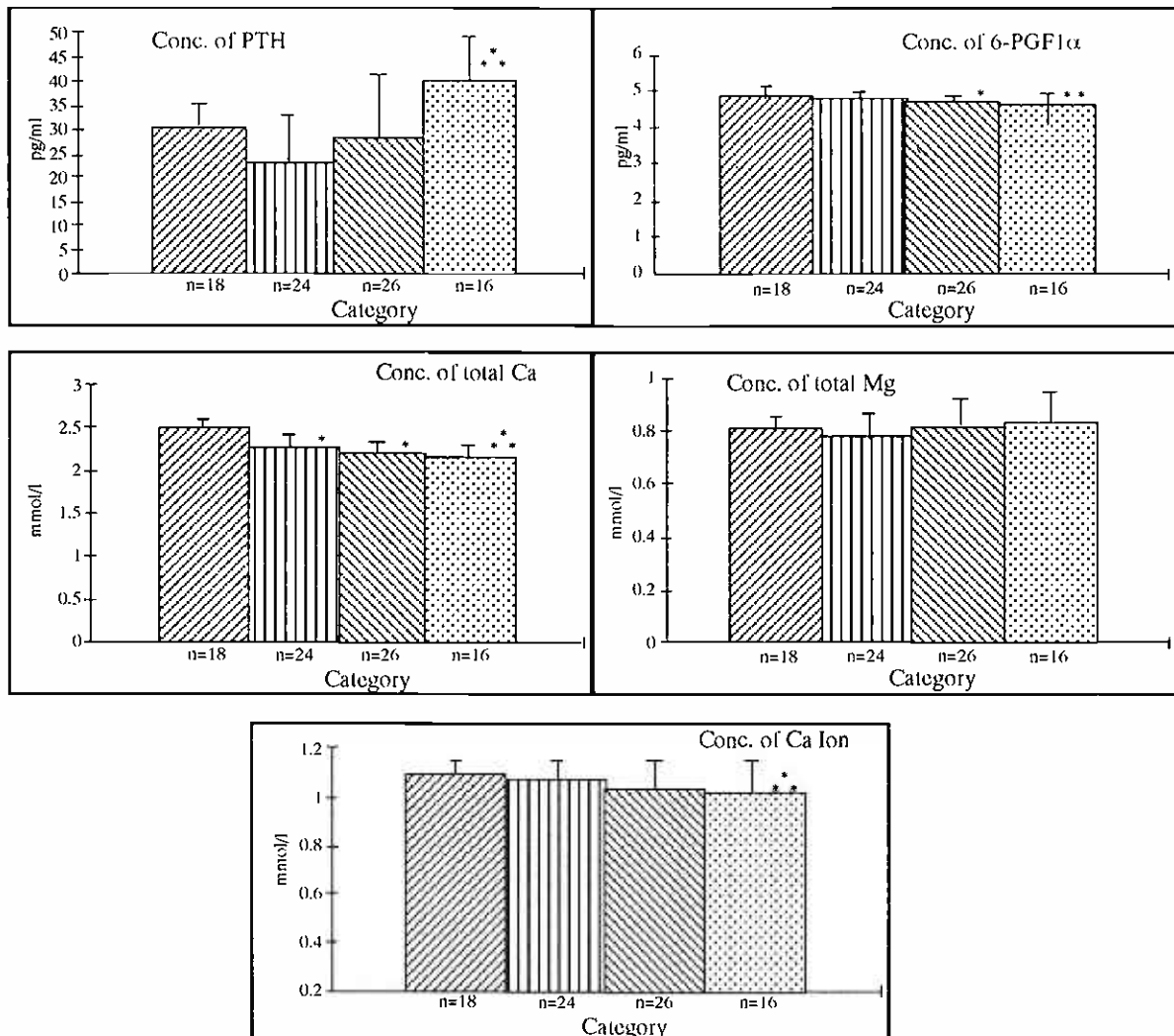
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**Fig 1 – Comparison of average total calcium, free calcium, total magnesium, parathyroid hormone (PTH), 6-keto-prostaglandin- $F_{1\alpha}$  values between four categories. The values are in mean  $\pm$  standard deviation (SD).**



Shading of bar chart for four categories: = non-pregnant normotensive (NNP), = pregnant normotensive (NP), = pregnancy-induced hypertension (PIH), = pre-eclampsia (PE). n = number of samples. Significant difference (p<0.05) was found when compared with NNP (\*) and NP (\*\*).

assay involved the use of  $^{125}I$  and intact PTH<sup>(8)</sup> was measured. Measurement of the 6-keto-PGF $_{1\alpha}$  level in blood plasma also required the use of a radioisotopic kit (Amersham International) which involved the use of  $^3H$ .

The data was analysed statistically by unpaired Student's-t test, regression and correlation tests. A p value <0.05 was considered significant.

## RESULTS

From this study, minerals, parathyroid hormone and 6-keto-prostaglandin- $F_{1\alpha}$  affect both pregnancy and hypertension. With reference to Fig 1, the following results were found. In pregnant normotensive women, total calcium and PTH levels were found to decrease (p<0.05), compared to non-pregnant normotensive women. In PIH patients, total calcium and 6-keto-PGF $_{1\alpha}$  levels decreased significantly (p<0.05) compared to subjects who were non-pregnant normotensive.

In pre-eclampsia patients, total calcium, calcium ion and 6-keto-PGF $_{1\alpha}$  levels decreased (p<0.05) while PTH level increased (p<0.05) compared to the non-pregnant

normotensive group. Total calcium and calcium ion levels decreased (p<0.05) while PTH level increased (p<0.05) when compared to the pregnant, normotensive women.

Calcium ion was found to be negatively correlated (NNP : r = -0.883, p=0.008 / NP : r = -0.931, p = 0.000) while PTH was positively correlated (NNP : r = 0.904, p = 0.013 / NP : r = 0.913, p = 0.000) with mean arterial pressure (MAP). Also, total magnesium had a positive correlation with PTH (r = 0.49, p = 0.039).

## DISCUSSION

In this study, for normal pregnancy, total calcium level was found to be decreased by 10% from the mean value of NNP subjects. This maybe due to the additional requirement of calcium for not only the mother, but also the foetus. Calcium ions are directly involved in the contraction of smooth muscles whereby the size of the lumen of the muscle affects blood pressure. Therefore, the better parameter to measure is the ionic calcium, not total calcium. The level of ionic calcium was also found to be significantly decreased in PIH and PE

**Table I - Distribution of samples within the four categories (mean±SD).**

Category	NNP	NP	PIH	PE
n (84)	18	24	26	16
Race: C/M/I	3 / 12 / 3	3 / 16 / 5	5 / 18 / 3	3 / 11 / 2
Age (years)	29.78± 8.68	29.33± 5.64	30.15± 7.93	30.13± 7.32
Weight (kg)	60.39±13.33	70.29±11.80	70.68±12.05	69.90± 8.80
Gestation (wks)	-	32.33± 3.94	33.12± 6.87	32.75± 3.49
MAP (mmHg)	78.22±18.88	85.55± 5.87	103.4±20.24	116.48±9.26

Key: NNP = non-pregnant, normotensive; NP = pregnant normotensive; PIH = pregnancy-induced hypertension; PE = pre-eclampsia; Race: C = Chinese, M = Malay, I = Indian; MAP = mean arterial pressure.

subjects as compared to both NNP and NP subjects. During PE, the capillary of the glomerulus was found to be more permeable to plasma protein<sup>(9)</sup>. This may partly explain the lower level of calcium ions seen in PE subjects in this study.

No significant change was found in the level of total magnesium in any of the categories studied. No change has been detected since the active form of magnesium, like calcium, is the ionic form not the total form<sup>(10)</sup>. It had been suggested that it is the ionic form of magnesium and calcium which will compete for the active site to bring about the suitable physiologic changes<sup>(11)</sup>. If there was any change in the ionic magnesium, this was not reflected by the level of total magnesium found in this study.

PTH level during normal pregnancy decreased significantly by 22% compared to NNP subjects. With the observation that total and ionic calcium also decreased in these subjects, dilution of these parameters in the plasma by expansion of plasma volume in normal pregnancy could be the explanation. There have been studies that reported findings of plasma volume expansion in NP subjects<sup>(12)</sup>.

For PIH, the PTH level was similar to the NNP level but increased compared to NP level. While for PE, the PTH level was significantly increased by 37% and 76% compared to NNP and NP levels respectively. On the other hand, ionic calcium was found to be decreased in both PIH and PE groups. Unlike NP condition, plasma volume expansion in PIH and PE were found to be decreased<sup>(13)</sup>. Thus, reduced ionic calcium is a true picture of a PE state. It remained low even though the PTH level was high, implicating that for the PE state, a higher PTH level was required to achieve a given level of ionised calcium to meet the foetal demand.

For the NNP and NP groups, ionic calcium was found to be negatively correlated with mean arterial pressure (MAP) while the reverse was observed for PTH. Studies of calcium supplementation to women with PIH demonstrated a reduction in their blood pressures after supplementation<sup>(14,15)</sup>. This suggests that abnormalities in calcium metabolism exist in PIH women and may contribute to their hypertension.

In PIH subjects, the level of 6-keto-PGF<sub>1α</sub> was found to be decreased by 4% and 2% from the NNP and NP levels respectively. This may be due to the disability of the umbilical arteries to produce enough prostacyclin<sup>(16)</sup>. A hypothesis suggested that this may be the result of a disorder in the endothelial function or immune complex that prevents the synthesis of prostacyclin (Pgl<sub>2</sub>) without affecting the synthesis of thromboxane (TxA<sub>2</sub>)<sup>(17)</sup>.

The level of 6-keto-PGF<sub>1α</sub> in PE subjects was also found to be significantly decreased by 6% as compared to NNP subjects. This result supports similar findings of other workers<sup>(18-20)</sup>. It has been suggested that the imbalance in Pgl<sub>2</sub> production in relation to TxA<sub>2</sub> production and restoration of normal Pgl<sub>2</sub>/TxA<sub>2</sub> ratio, which is decreased in PE, is the

rationale for low-dose aspirin therapy in these patients<sup>(20,21)</sup>.

## CONCLUSION

This study showed that a definite pattern of change occurs in the levels of calcium, magnesium, PTH and 6-keto-PGF<sub>1α</sub> in subjects with PIH and PE. Our Malaysian results on serum PTH and ionized calcium as well as plasma 6-keto-PGF<sub>1α</sub> in PIH and PE patients support the findings of Western workers.

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