MINERAL AND PARATHYROID HORMONE INTER-RELATIONSHIPS IN NORMAL PREGNANCY AND PREGNANCY-INDUCED HYPERTENSION

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ABSTRACT

The serum of calcium, other involved minerals and parathyroid hormone (PTH) were studied in non-pregnant women, during pregnancy and in pregnancy-induced hypertension (PIH). In pregnant women, serum creotinine, total calcium, total protein, albumin, inorganic phosphorus and magnesium declined, while parathyroid hormone levels increased significantly when compared to non-pregnant women. In PIH cases, serum total proteins, albumin and inorganic phosphorus were further reduced, while PTH levels were further increased when compared to normal pregnant women. Serum ionised calcium and sodium levels were similar in all the three groups. No significant relationship between blood pressure, PTH and involved minerals was observed in this study (JPMA 43: 92. 1993).

INTRODUCTION

The physiologic, biochemical and anatomic Changes during pregnancy are extensive and may be systemic or local. However, most systems return to pre-pregnancy status between the time of delivery and 6 weeks post partum[1,2]. Hypertensive states in pregnancy include pre-eclampsia-eclampsia (pregnancy induced hypertension), chronic hypertension, chronic hypertension with super-imposed pre-eclampsia or transient hypertension[3,4]. The term pre-eclaxnpsia is criticized because only a small proportion of the patients develop eclampsia and the term pregnancy-induced hypertension is now used[3]. Pregnancy-induced hypertension (PIH) with proteinuria occurs in 2-4% of primigravidae and hypertension without proteinuria in 15-20%. The predisposing factors for PIH are nulliparity, black race, maternal age below 20 or over 35 years, low socio-economic status, hydatiform mole, polydramnios, non-immune fetal hydrops, diabetes, chronic hypertension and underlying renal disease. The physiologic state of pregnancy is associated with significant placental transfer of calcium and phosphorus necessary for mineralization of the fetal skeleton. The maternal adjustments in calcium metabolism, other involved minerals and calcium regulating hormones have been studied by different workers[5-9]. An inverse relationship between PIH and calcium intake has been reported[10-12]. The mineral and parathyroid hormone inter- relationships in normal pregnancy and PIH can characterize these physiologic adjustment and reflect some light on casual role of calcium in the pathogenesis of PIH. The extent of physiologic hyperparathyroidism in normal pregnancy and that occurring in pregnancy-induced hypertension has not so far been studied in Pakistan. The present work was, therefore, carried out to study the serum levels of calcium, other involved minerals and parathyroid hormone (PTH) in normal pregnancy, pregnancy-induced hypertension and in non-pregnant women and to investigate the possible relationship, if any, between these minerals and PIH and their probable role in normal pregnancy and pregnancy-induced hypertension.

PATIENTS AND METHODS

The study included 100 women (age range 18-40 years) receiving obstetric and gynaecologic care at the outpatients departments of Jinnah Postgraduate Medical Centre, Civil Hospital and Sindh Government Lyari General Hospital, Karachi. The subjects were classified into the following groups: a) normal non-pregnant women (30 cases), b) normal pregnant women, 3rd trimester (35 cases) and c) pregnancy-induced hypertensive women, 3rd trimester (35 cases). The controls were age, parity and gestational age matched with PIH cases. The inclusion criteria for non-pregnant and pregnant women was: blood pressure always <140/90 mmHg or a rise, if any, always <20 mmllg, above the previously existing diastolic pressure, normal renal function as assessed by serum creatinine and no asymptomatic bacteriuria as assessed by urine microscopy. Criteria for pregnancy-induced hypertensive women were normal blood pressure before the 20 weeks of pregnancy but persistently elevated to atleast 140/90 mmHg or a rise >20mmHg above the previously existing diastolic pressure, normal renal function and no asymptomatic bacteriuria. The exclusion criteria were: pregnant women having twins, women suffering from chronic hypertension and non-pregnant/pregnant women taking calcium supplementation. The detailed history including obstetric history and complete physical examination of all the subjects was carried out using standard instruments and recorded on a specially designed proforma. The blood pressure measurements were made in supine position, in triplicate and the average of these three readings was taken as the representative value for that subject. About 10 ml of blood was drawn, by an asceptic antecubital venipuncture, into a vacuum glass tube (Terumo) without additives. Serum was separated after one hour (3000 rpm for 10 minutes) and kept in 4 small, capped, plastic tubes at -20°C until analysis. The samples were allowed to attain room temperature before any determination was carried out. Total serum proteins were estimated by Biuret method[13], serum albumin by Bromo-cresol-green method[14], serum creatinine by Ralston method[15], serum total calcium by 0-Cresolphtalein complexone method[16], serum magnesium by the method of Mann and Yoe[17], while serum inorganic phosphorus was estimated by Fiske and Subbarow method[18]. Serum sodium was estimated by flame photometry[19] using corning 405 model flame photometer, while serum parathyroid hormone was determined by radioimmunoassay[20] using MM-hPTH RIA kit, code IBM 800 from Amersham International PIC. Serum ionized calcium was calculated by the use of Zeisler' s[21] formula:
2+ 6Ca—P/3 mgCa /dl P+6
where Ca — total calcium and P = total protein. Midstream daytime urine samples were collected in clean, wide mouthed glass bottles[22] and checked for proteinuria, glycosuria and bacteriuria to ensure absence of diabetes and urinary tract infection. The detection of proteins and glucose in urine was made using MultistixAmes reagent strips[23]. About 5 ml of urine was taken in a clean glass tube and centrifuged at 1000-1500 rpm for 5-10 minutes. The supernatant was discarded and a drop of sediment was placed on a slide, then covered with a coverslip and observed under microscope (1:40) for bacteria, WBCs, epithelial cells, casts and crystals. The data were analyzed by applying students 't' test for group comparison[24] and the inter-relationship and relationship between two variables were analyzed for calculating correlation coefficient 'r' and regression lines respectively[24].

RESULTS

The data regarding age, height, weight, parity, gestational age and blood pressure is shown in Table I.

TABLE I. Age, parity, gestational age and blood pressure in three study groups Mean ± S.E..

Groups	Age (years)	Height (cm)	Weight (kg)	Parity (No.)	Gestational age (weeks)	Blood pressure (mmHg) Systolic	Diastolic
A. Non-pregnant	29.43	153.70	57.05	3.43	-	108.20	68.33
women (30)	±1.00	±1.16	±2.14	±0.45		±1.77	±1.36
B. Pregnant	28.06	153.73	61.27	2.71	33.00	110.17	69.89
women (35)	±1.00	±1.59	±1.94	±0.46	±0.53	±1.62	±1.28
C. Pregnancy-	28.63	154.83	69.19*	2.83	33.46	151.80**	97.69**
induced hypertensive women (35)	±1.06	±1.47	±2.41	±0.52	±0.60	±2.57	±1.11

Number of cases is given in parenthesis.
* P < 0.02 as compared to pregnant women.
**P < 0.001 as compared to non-pregnant and pregnant women.

The body weight and the systolic and diastolic blood pressure levels were significantly higher in group C when compared with the two control groups A and B. The total protein, albumin and A/G ratio were significantly reduced in both groups B and C, while creatinine was reduced only in group B, when compared with group A. Serum creatinine, total protein, albumin and A/G ratio were all significantly lowered in group C in relation to group B (Table II).

TABLE II. Serum creatinine and protein values in three study groups Mean ± S.E.

Groups	Creatinine (mg/dl)	Total protein (g/dl)	Albumin (g/dl)	A/G ratio
A. Non-pregnant	0.79	7.84	4.88	1.68
women (30)	±0.02	±0.09	±0.05	±0.05
B. Pregnant	0.64***	7.07***	4.08***	1.39***
women (35)	±0.01	±0.12	±0.06	±0.03
C. Pregnancy-induced	0.75###	6.62#***	3.62###***	1.22##***
hypertensive women (35)	±0.03	±0.14	±0.10	±0.04

Number of cases is given in parenthesis.
*** P < 0.001 as compared to non-pregnant women.
# P < 0.02 as compared to pregnant women.
P < 0.01 as compared to pregnant women.
P < 0.001 as compared to pregnant women.

Parathyroid hormone (PTH) increased while total calcium decreased in group B and C when compared to group A while serum ionized calcium levels are similar in all three groups. Serum PTH levels are further elevated in group C in comparison with group B (Table III).

TABLE III. Serum parathyroid hormone, calcium and other minerals in three study groups Mean ± S.E.

Groups	Parathyroid hormone (pmol/l)	Total calcium (mg/dl)	Ionized calcium (mg/dl)	Magnesium (mg/dl)	Inorganic phosphorus (mg/dl)	Sodium (mEq/l)
A. Non-pregnant women (30)	52.99 ±2.12	8.73 ±0.12	3.60 ±0.05	2.13 ±0.50	3.02 ±0.05	137.73 ±0.48
B. Pregnant women (35)	62.13** ±2.74	8.11** ±0.20	3.54 ±0.09	1.90** ±0.06	2.58 ±0.06	138.17 ±0.39
C. Pregnancy-induced hypertensive women (35)	73.88##*** ±2.86	7.95*** ±0.20	3.61 ±0.09	2.47 ±0.52	2.26###*** ±0.06	138.94 ±0.89

Number of cases is given in parenthesis.
** P < 0.01 as compared to non-pregnant women.
*** P < 0.001 as compared to non-pregnant women.
P < 0.01 as compared to pregnant women.
P < 0.001 as compared to pregnant women.

Serum inorganic phosphorus levels show a significant fall in pregnancy (group B and C) while serum magnesium is significantly lowered only in group B, the serum sodium levels are similar in all the groups. The degree of association of calcium and other involved minerals with PTH is presented in Table IV.

TABLE IV. Degree of association of calcium and other involved minerals with parathyroid hormone.

Groups	Total calcium	Ionized calcium	Inorganic phosphorus	Magnesium
	Correlation coefficient 'r' values			
A. Non-pregnant women (30)	-0.40*	-0.48***	-0.02	0.06
B. Pregnant women (35)	-0.61***	-0.53**	0.24	-0.31
C. Pregnancy-induced hypertensive women (35)	-0.24	-0.004	0.03	-0.21

Number of cases is given in parenthesis.
* P < 0.05; ** P < 0.01; *** P < 0.001

The serum PTH levels were significantly negativelyrelated with total calcium and ionised calcium in groups A and B. In group C none of the involved minerals showed any significant correlation with PTH. The degree of association between blood pressure, PTH and involved minerals in the three groups is presented in Table V and VI.

TABLE V. Degree of association between systolic blood pressure, parathyroid hormone and involved minerals.

Groups	Parathyroid hormone	Total calcium	Ionized calcium	Inorganic phosphorus	Magnesium	Sodium
	Correlation coefficient 'r' values					
A. Non-pregnant women (30)	0.067	0.104	0.009	0.230	-0.246	0.104
B. Pregnant women (35)	-0.005	0.074	0.149	-0.163	0.158	0.095
C. Pregnancy-induced hypertensive women (35)	0.133	-0.098	-0.029	0.144	-0.010	-0.053

Number of cases is given in parenthesis.
All the correlations are weak and statistically non-significant.

TABLE VI. Degree of association between diastolic blood pressure, parathyroid hormone and involved minerals.

Groups	Parathyroid hormone	Total calcium	Ionized calcium	Inorganic phosphorus	Magnesium	Sodium
	Correlation coefficient 'r' values					
A. Non-pregnant women (30)	0.092	0.156	0.035	0.172	-0.026	0.015
B. Pregnant women (35)	0.082	-0.074	-0.048	-0.154	0.240	0.076
C. Pregnancy-induced hypertensive women (35)	0.128	-0.108	-0.108	0.230	-0.257	-0.097

Number of cases is given in parenthesis.
All the correlations are weak and statistically non- significant.

All the correlation co-efficients are weak and statistically non-significant.

DISCUSSION

Concentration of total calcium in maternal serum characteristically declines during pregnancy[25,26]. Present work showed similar trends in pregnant women. This decline, also shown in this study, involves the protein-bound portion as evidenced by the very strong positive correlation between total calcium and albumin levels[27]. A highly significant correlation coefficient of 0.68 (PczO.001) in group A and 0.46 (P<0.01) in group B between total calcium and albumin levels was observed. However, this coefficient had a low and non-significant value of 0.29 in group C The decrease in serum total calcium in group B as compared to group A is in agreement with the data of Pitkin[1] and Varner[27], however increasing trends have been reported by Drake[9]. Present study also showed a reduction in serum inorganic phosphorus and magnesium levels for groups B and C. Olatunbosun et al[6] and Reitz et al[26] have observed a significant decrease in these minerals in the latter half of pregnancy when compared with the first half, while Pitkin et al[1] and Varner et al[27] reported a non-significant correlation between magnesium, inorganic phosphorus and the duration of pregnancy. Maternal serum PTH levels increase

during normal gestation, especially during third trimester of pregnancy[1,9,26,28]. In the present study, a markedly significant higher level was observed in group B as compared to group A- However, these raised serum PTH levels were still within the normal range (40-100 pmol/l) and compatible with the findings of Drake[9] and Pitkin[1]. The exact mechanism involved in the inverse relationship between serum calcium and blood pressure is not clearly understood. Recently PTH has been suggested to be involved in this relationship[10,12,30,31]. The steps of this hypothesis are best explained by Belizan et al[10] and Repke et al[11]. In the present study, in 97 percent of the group C cases (34/35), the serum PTH levels were still within the normal range. Even, the one remaining case, showed only a marginal increase, which is well within the range of error of estimation of PTH. The correlation coefficients of both serum total calcium and ionised calcium with serum PTH are weak and statistically non-significant in group C, although they show inverse and significant correlations with PTH in groups A and B. The correlation coefficients between blood pressure, PTH and involved minerals were found to be weak and non-significant in all the three experimental groups and do not support the probable role of PTH and involved minerals in affecting blood pressure levels in the three groups in the present study. It may, therefore, be concluded that results of the present study do not confirm the hypothesis that pregnancy-induced hypertension is mediated through a control of serum PTH, total calcium and ionized calcium levels.

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