Does serum calcium in pre-eclampsia and normal pregnancy differ?

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ABSTRACT

Objective: To determine the calcium and parathyroid hormone levels in normal pregnancy and pregnancy induced hypertension.

Methods: Eighty pregnant women were enrolled in this study, 50 women represented the study group (Pregnancy-induced hypertension), and 30 women represented the control group (normal pregnancy). This study was carried out between March 1998 to February 2000 at King Hussein Medical Center, starting from the first or 2nd trimester. Once the patient developed hypertension for the first time in the 3rd trimester and fullfilled the selected criteria she was enrolled in this study.

Results: The mean serum total calcium of the study group was (8.22+/-0.12mg%), while the mean serum total calcium of the control group was (9.50+/-0.16mg%). There was a statistical significance between the 2 groups, lower in the study group P<0.005. Serum parathyroid hormone concentration was significantly higher in the study group P< 0.005.

Conclusion: It has been widely documented that there is a relationship between low calcium level and pregnancy induced hypertension. Our study suggests that maternal serum total calcium and parathyroid hormone be related to pregnancy-induced hypertension. The low level of maternal total calcium may have a role in the development of this disorder in pregnancy, therefore calcium supplementation during late pregnancy may be used to help in the prevention of this disorder. However, to date there is still no evidence regarding this supplementation and there are no available reports conclusively demonstrating the actual mechanism.

Keywords: Calcium, parathyroid hormone, pregnancy induced hypertension.

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The presence of chorionic villi in certain women incites vasospasm and hypertension. Hypertensive disorders complicating pregnancy are common and form one of the great triad, along with hemorrhage and infection, that continues to be responsible for a large number of maternal deaths. However why pregnancy incites or aggravates hypertensive vascular disease remains unsolved, despite decades of intensive research, and these disorders remain among the most important unsolved problems in obstetrics.[1] Recently, it has been suggested that there is an association between calcium intake and pregnancy-induced hypertension (PIH).[2] Women with low calcium intake have an increase in mean blood pressure which predisposes them to the development of (PIH) during the last part of gestation.[3] The explanation for this process is not clear. The low level of maternal total calcium is due to an increase in the fetal calcium demand,[4] and is due to an increase in maternal estrogen production which blocks bone resorption which increases calcium excretion in urine, and thus aggravates the situation.[5] Parathyroid hormone (PTH) as a compensatory mechanism, tends to increase progressively, reaching a maximum level at term. Parathyroid hormone will increase intestinal absorption of calcium as the only compensatory process during pregnancy. Thus, the 3rd trimester of

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pregnancy is a hyperparathyroid state that maintains calcium levels within their physiologically narrow limits. If calcium supplementation is provided, particularly late in pregnancy, this hyperparathyoid state may be reduced.[6] The elevation of parathyroid hormone causes an increase in free intracellular ionized calcium, which results in vasoconstriction and a rise in the blood pressure.

Methods. This study was carried out at King Hussein Medical Center in the period from March 1998 to February 2000. Eighty pregnant women were enrolled in this study, 50 women represented the study group and 30 women represented the control group.

Study group (selection criteria). 1. Pregnant females with a singleton pregnancy. 2. Age range between 15 and 40 years. 3. Gestational age: All in the 3rd trimester, the gestational period ranged from 30 to 42 weeks calculated from the first day of the last menstrual period. 4. All primigravidae. 5. All diagnosed to have PIH based on the development of hypertension in the 3rd trimester for the first time, proteinuria with or without edema. 6. No history of previous urinary tract troubles and no evidence of UTI (urinary tract infection). 7. Not diabetic.

Control group. The women representing the control group were chosen from other women who fulfill the same previously mentioned criteria but who did not develop hypertension during the 3rd trimester. They were all normotensive, with a systolic blood pressure of 130 mmHg or less and a diastolic blood pressure of 80mmHg or less. All findings were recorded, tabulated and statistically analyzed using, paired t-test, chi-square test and the r-test on an IBM-XT computer using the Microstat package, Version III program. The women included in this study were followed up in the outpatient clinic of the hospital, starting from the first or the 2nd trimester as booking clients. On development of hypertension for the first time in the 3rd trimester and fulfillment of the selection criteria they were enrolled in the study group. The following steps were taken during the study: 1. History was taken to be sure that the patient had fulfilled the selection criteria. 2. A thorough clinical examination was carried out. 3. To diagnose hypertension, the blood pressure was measured by the sphygmomanometer while the patient was lying on a couch on her side. The reading should be 140/90 mmHg and above. 4. To diagnose proteinuria, 2 midstream samples of urine collected at least 4 hours apart showing albumin "+" or more using reagent strips or dipstick. 5. Urinary tract infection was excluded by routine urine analyses. 6. Diabetes mellitus was excluded by fasting blood sugar. 7. Measurement of calcium in serum by quantitative calorimetric method, which was based on the direct combination of calcium with reactant orthocesolphthalein complex (OCPC), to form a stable, colored reaction product. 8. Measurement of parathyroid hormone in serum. 9. Both the study group and the control group were followed up until delivery and the outcome of pregnancy was evaluated as regards sex, weight and estimated apgar score at one and 5 minutes.

Results. The difference in clinical variables between the 2 groups are shown in Table 1. There was no statistical difference between the 2 groups for age or gestational period. The results showed that both systolic and diastolic blood pressure values were significantly higher in the study group when compared with the control group. Mode of delivery and outcome of pregnancy of the 2 groups are shown in Table 2, and there was no statistical significant difference in the mode of delivery of both groups.

Table 1 - Different variables in both the control group and the study group.

Clinical Data	Control Group n=30	Study Group n=50	Significance	P-value
Blood pressure				
Systolic	111.20 ± 6.39 mmHg	171.20 ± 20.88 mmHg	S	P<0.05
Diastolic	75.33 ± 5.16 mmHg	104.80 ± 10.84 mmHg	S	P<0.05
Age	23.40 ± 2.94 years	25.04 ± 5.10 years	NS	P>0.05
Gestational Age	37.00 ± 2.69 weeks	36.76 ± 3.15 weeks	NS	P>0.05
Weight	3.196 ± 0.265 kg	2.992 ± 0.263 kg	S	P<0.05
Serum calcium level	9.50 ± 0.16 mg%	8.22 ± 0.12 mg%	S	P<0.005
PTH level	36.11 ± 8.91 ng%	43.30 ± 7.03 ng%	S	P<0.005

S=statistically significant, NS=statistically non-significant,
PTH= parathyroid hormone, n=number

Table 2 - Mode of delivery and the outcome of pregnancy in both control and study groups.

Clinical Data	Control Group n=30	Study Group n=50	Significance	P-value
Mode of delivery:				
NVD	20	32	NS	P>0.05
Instrumental	6	8	NS	P>0.05
C/S	4	10	NS	P>0.05
Products of conception:				
Sex	14M 16F	24M 26F		
Sex ratio	(1.1:1)	(1.08:1)		
Apgar score at one minute	8.93 ± 0.96	7.16 ± 0.85	S	P<0.005
Apgar score at 5 minutes	9.86 ± 0.87	9.24 ± 0.87	S	P<0.05

M=male, F=female, S=statistically significant, NS=statistically non-significant, NVD=normal vaginal delivery, C/S=cesarean section, n=number

The weight of the newborns of the study group ranged from 2.200 kg to 3.500 kg while the weight of the newborns of the control group ranged from 2.850 kg to 3.700 kg. There was significant low birth weight in the study group as compared with the control group as shown in Table 1. The Apgar score for the newborns of the study group at one minute ranged from 7 to 9 and at 5 minutes from 7 to 10. While the Apgar score of the newborns of the control group at one minute ranged from 9 to 10. There was a significant lower Apgar score at one minute and 5 minutes in the study group of P<0.005 and P<0.05, as shown in Table 2. As regards serum calcium, in the study group it was ranged from 8.00 to 8.80mg%, while in the control group serum calcium was ranged from 9.40 to 9.80. There was a statistical significant difference between the 2 groups, being lower in the study group compared with the control group (Table 1). As regards serum PTH, the study group ranged from 30.97 to 58.35ng%, while the control group, serum PTH ranged from 23.10 to 53.29ng%. The result of parathyroid hormone level is significantly higher in the study group P<0.005.

Discussion. Calcium, is one of the most abundant elements in the human body and serves a variety of vital functions. Pregnancy entails a number of physiologic events with implications regarding calcium metabolism; the extracellular fluid expands, the albumin level decreases, the glomerular filtration rate increases causing increase in calciuria and calcium is removed from the maternal system by transfer to the fetus. These mechanisms all tend to promote lowering of maternal calcium concentration.[7] Adjustment in calcium metabolism seems to involve increasing PTH activity, PTH levels may decline in early gestation but in any event a progressive increase in secretion characterizes the last 2 3rds of pregnancy, which enables the pregnant woman to maintain essentially constant serum calcium levels.[8] Maternal bone calcium tends to be preserved during pregnancy as the bone response to PTH seems to be diminished due to a blockade effect of increasing estrogen also the response to calcitonin is enhanced with the aim of protecting the maternal skeleton from excessive calcium resorption during hypercalcemic periods.[9] Maternal intestinal absorption of calcium can increase from 27% before pregnancy to as high as 50% during gestation.[10] The role played by calcium in the pathogenesis of pregnancy induced hypertension is nowadays receiving growing interest, and the studies carried out on this subject revealed conflicting results. Our study has shown that maternal levels of PTH increased above the lower limit of the non-pregnant levels in both groups (12ng%-72ng%) but it is significantly higher in the study group than the control group. Ohara et al reported similar observations, where he found a significant increase of PTH in severe pregnancy-induced hypertension.[11] The increased level of PTH in both groups is due to the following: 1. The growing fetus which demands calcium of approximately 30 grams at term.[12] 2. The increase in GFR 3. The increase in estrogen level, thus lowering calcium.[13] Our study has shown that maternal total serum calcium levels can be significantly lower in pregnancy-induced hypertension than in normal pregnant women, these results are in accordance with the findings of Belzan et al.[3] As regards the outcome of pregnancy, both groups showed a significant difference in the birth weight of 204gms, P<0.05. Apgar score at one minute equals P<0.005 and 5 minutes P<0.05, this is in accordance with the findings of Sibai et al.[14] For birth weight, as hypertensive disorders during pregnancy are associated with vasculopathy, which also affects the

placenta, the relative placental insufficiency would be expected to affect the fetal birth weight to some degree. These results are in co-ordinance with the results of Andersh et al.[15] Lower apgar scores are therefore due to the effect of the disease itself on the fetal circulation.

In conclusion, it has been widely documented that there is a relationship between low calcium level and pregnancy induced hypertension. Our study suggests that maternal serum total calcium and PTH are related to PIH. The low level of maternal total calcium may have a role in the development of this disorder in pregnancy, therefore calcium supplementation during late pregnancy may be used to help prevention. However, to date there is still no evidence regarding this supplementation and there are no available reports conclusively demonstrating the actual mechanism. More studies should be carried out in this field.

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