Comparison of serum calcium, total protein and uric acid levels between hypertensive and healthy pregnant women in an Iranian population

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Abstract: The objective of this study was to compare serum calcium, total protein, and uric acid levels between hypertensive and healthy pregnant women. In this cross-sectional study, 100 healthy and 48 hypertensive pregnant women with singleton pregnancy who were at ≥ 28 weeks of gestation were included and serum calcium, total protein, and uric acid levels were compared between these two groups. Hypertensive group consisted of 28 subjects with mild preeclampsia, 17 with severe preeclampsia. Mean (±SD) serum calcium level was 7.88 (±0.94) mg/dl (range, 6.94-8.82) in hypertensive and 8.28 (±0.77) mg/dl (range, 7.51-9.05) in control group (P = 0.01). Mean (±SD) serum total protein level was 6.023 (±0.91) gr (range, 5.32-7.14) in hypertensive and 6.13±0.77 (5.36-6.9) in control group (P > 0.05). Mean (±SD) level of serum uric acid was 5.32 (±1.41) mg/dl (range, 3.91-6.73) in hypertensive and 4.55 (±1.14) mg/dl (range, 3.41-5.09) in control group (P = 0.001). Mean serum Ca level was significantly lower in hypertensive pregnant women in comparison with healthy ones. Considering this factor in prenatal care is important.

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1. Introduction

Hypertensive disorders in pregnant women are one of the major factors that cause high risk pregnancy and fetal and maternal morbidity. These disorders are most seen in primiparas and are reported in 10% of pregnancies. Early diagnosis of these disorders is a way of reducing maternal and neonatal morbidity/mortality (1-8). Epidemiological evidence suggests changes in the metabolism of calcium (Ca) as a responsible factor in the path physiology of preeclampsia. Hence, decreased in Ca intake may result in progression of preeclampsia to eclampsia (5, 6, 9).

There have been efforts to recognize a useful laboratory test to predict prognosis of hypertensive women in pregnancy. In a meta-analysis by Thangaratinam et al. on the level of uric acid during pregnancy, it was concluded that this factor is not an accurate predisposing factor. This finding agrees with the data reported by Cnossen et al. (10, 11). In another study, it was noted that severe preeclampsia and eclampsia were accompanied by decreased levels of serum Ca and total protein and on the other hand increased level of serum phosphorus (5). Likewise, lower serum Ca and higher uric acid levels were reported in pregnancy-induced hypertension (PIH) compared to normotensive women (6). A significant correlation between serum Ca and hypertension has been shown in PIH (7). It has been reported that patients with high risk pregnancies (e. g., risk of progressive hypertension and those with low amounts of dietary Ca) can benefit from Ca supplementation (8). Regarding the aforementioned data we decided to measure the serum levels of Ca, total protein, and uric acid in a sample of hypertensive women in pregnancy.

2. Material and Methods

This cross-sectional study was done at Shariati Hospital, Bandar-Abbas, southern of Iran. One-hundred healthy pregnant women were entered into the study and were compared to 48 hypertensive pregnant women. All subjects were at 28 weeks of gestation or more at the time of entry and the subjects of the two groups were matched regarding age and parity and BMI. All cases had singleton pregnancy. Exclusion criteria were overt and/or gestational diabetes mellitus, nephropathy, glumerolopathy, and history of hypocalcaemia.

Hypertension was defined as blood pressure (BP) over 140/90 mmHg which was measured in two separate occasions six hours apart. Hypertensive women were categorized as following. Preeclampsia is defined as blood pressure (BP) of at least 140/90 mmHg after 20th week of gestation accompanied by proteinuria of at least 300 mg per 24 hours in previously normotensive women. The patients with

systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 on two occasions with proteinuria equal or more than 2 grams in 24 hour urine sample or any of severe preeclampsia's criteria including oliguria (urine volume less than 500 cc per 24h), Thrombocytopenia (platelet count less than 100000), raised liver enzymes; aspartate aminotransferase (SGOT) > 50 U/L or alanine aminotransferase (SGOT) > 60 U/L , epigastric pain, pulmonary edema, visual or brain function disturbance or intrauterine growth restriction of the fetus were considered as severe preeclampsia. Eclampsia is recognized by occurrence of seizure in preeclampsia that is not correlated with other causes. Predesigned checklists were used to gather required data. The checklist had two parts. The first part consisted of questions regarding age, gravidity, gestational age, underlying disease, cause of admission, and history of hypertension. The second part included data regarding results of measuring serum levels of Ca, total protein, uric acid, complete blood count (CBC), fasting blood glucose (FBS), and urine analysis which these blood samples were performed in third trimester of pregnancy (≥ 28 weeks of gestation) at time of admission before termination of pregnancy. All subjects were followed up for 48 hrs after delivery. Analysis of data was done using the SPSS Software for Windows (Ver. 16.0). The quantitative data were compared between the two studied groups by the student t-test. Significant level was set as $P < 0.05$.

3. Results

Mean (±SD) age of control group was 26.6 (±6.73) years and in hypertensive this figure was 27.96 (±6.25) years. The oldest subject in control group had 43 years of age and in hypertensive had 44 years of age. The two groups were not different in terms of their mean age (Table 1). Mean (±SD) gestational ages in control group and hypertensive were 38.37 (±2.12) weeks and 36.06 (±4.46) weeks, respectively ($P = 0.008$). In hypertensive group, 28 subjects (53.9%) had preeclampsia, 17 subjects (32.7%) had severe preeclampsia, and three subjects (0.97%) were diagnosed by eclamptic. Mean (±SD) blood platelet levels in control group and hypertensive were 229×103 (±72.3×103) vs. 191×103 (±80.5×103) ($P = 0.005$). Mean (±SD) hemoglobin levels were 11.61 (±1.99) g/dl in control group and 11.85 (±1.32) g/dl in hypertensive (Table 1). Mean (±SD) serum Ca levels in control group and hypertensive were 8.28 (±0.77) mg/dl and 7.88 (±0.94) mg/dl, respectively ($P = 0.01$). Table 3 presents the measured laboratory indices in the two groups. This study demonstrated very significant correlation between serum uric acid level and type of hypertensive disorder ($p<0.05$).

Table 1. Mean serum calcium, protein and uric acid to separate the blood disorder

Groups	Control	Mild preeclampsia	Severe preeclampsia	Eclampsia	P value
Number	100	8.28 ± 7.6	6.13 ± 5.1	4.54 ± 4.2	
Serum Ca levels (mg/dl)	28	7.88 ± 6.1	6.28 ± 4.5	5.04 ± 4.6	0.01
Total protein (gr/dl)	17	7.86 ± 6.6	6.15 ± 4.8	5.30 ± 4.5	NS
Serum uric acid level (mg/dl)	3	7.30 ± 6.7	5.63 ± 4.7	7.26 ± 5.2	0.001

Data are shown as mean±SD; NS: Not significant (Pvalue > 0.05)

4. Discussions

In this study serum Ca, total protein and uric acid levels in healthy pregnant women (100 cases) and hypertensive pregnant women (48 cases) were measured and compared Considering that mean of gestational age in control group was 38.37 (±2.12) weeks and in hypertensive group was 36.06 (±4.46) weeks, it can be concluded that pregnant women of this region postpone prenatal care for near the end of pregnancy except those who have disorders like hypertension. Serum Ca level difference was statistically significant between the two groups. Most studies on this issue confirm that high serum Ca level in pregnancy can lead to decreased incidence of preeclampsia (1, 5-7, 12-16). Multiple interventional studies have assessed the effect of Ca by prescribing variant types of Ca included diets in pregnant women. It has been noted that such dietary regimens can be effective in reducing BP and hypertensive disorders (8, 17-19). Ca supplements (1.5-2 gr as cacarbonate) have been prescribed for prevention of pregnancy disorders and their benefits have been proven in some investigations (20, 21). A study that reviewed 12 clinical trials also demonstrated that Ca supplements can lead to reduction in PIH in comparison with placebo (22). Other study

demonstrated that serum Ca level in healthy pregnant women did not have any statistically significant difference in comparison with pregnant women who suffered from hypertensive disorders and low level of Ca could not be the cause of hypertension and related disorders in pregnancy (10, 23-26). One of the causes might be diet consisting of calcium and territorial condition of Iran. The condition is sunny and the diet include dairy. A clinical trial consisted of 4589 nulipar pregnant women in 13-21 gestational age showed that Ca has no more effect rather than placebo on PIH (27). Mehri et al.(28) and Eini et al. (29) established that serum Ca level has no obvious difference in hypertensive women compared to healthy ones and Ca included dietary regimens cannot prevent from progression of preeclampsia. Vancho et al. reported that Ca included regimens are not useful for diminishing the severity of preeclampsia if the Ca level is not low as enough for presence of preeclampsia (30). Positive effect of mother's serum Ca in breastfeeding ability amelioration has also been mentioned (9). We found that serum total protein cannot be a predictive factor for preeclampsia incidence, because its difference in the two groups was not significant. This observation is similar to that of Salari et al. study (23). But this result was in contrast to Shahverdi et al. finding (5). Difference observed with respect to serum uric acid level between the two groups was significant and its level was higher in hypertensive women. In Almasganj et al. study, that serum uric acid level in healthy pregnant women was compared with hypertensive pregnant women, similar result was found. Significant lower platelet count in hypertensive women is the result of thrombocytopenia in patient with PIH. Abbasnik et al. carried out a study and compared blood platelet levels in preeclampsia and healthy pregnant women. They demonstrated that platelet level was obviously higher in healthy women than preeclampsia patients (31). Due to our findings we can conclude that serum Ca level in patients with hypertensive disorders is lower than healthy pregnant women and this result showed that hypocalcaemia can accompanied by hypertensive disorders during pregnancy. According to most studies, dietary regimens which include Ca can prevent hypertensive disorders, so administration of Ca supplements can minimize these disorders. Considering there are not enough studies assessing serum total protein levels and there was no difference between the two groups regarding this factor, serum total protein level cannot be a strong predictive factor to diagnose hypertensive disorders during pregnancy. Our study and another study (6) showed that uric acid levels are high in hypertensive patients. But Thangaratinam et al. (32) concluded from a meta-analysis that uric acid level measurement in pregnant women is not a strong predictive factor. Different references declared that serum Ca level diminishes during the third trimester of pregnancy (1). On the other hand there is a rising necessity of Ca during this trimester. Considering high prevalence of preeclampsia in our country(33) and especially in our study area, Bandar-Abbas- Iran special attention to nutritional conditions of pregnant women seems warranted. According to what mentioned in this article and necessity of special attention on this issue, we suggest:

1. Prospective studies with larger sample size and finding more factors for earlier diagnosis of hypertension in pregnancy.
2. Special attention to nutritional condition in pregnant women particularly in geographical regions that prevalence of malnutrition is high.
3. Educating pregnant women about nutrition during pregnancy and informing them about probable risks of inappropriate diet.

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