Serum Calcium, Phosphorous and Alkaline Phosphatase levels in Different Trimesters of pregnancy

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بررسی سطح کلسیم، فسفر و آلکالن فسفاتاز سرم در سه ماهه های مختلف حاملگی

خلاصه

مقدمه: اسکلت جنین درحین حاملگی شکل می گیرد و کلسیم و فسفر مورد نیاز به وسیله مادر تامین می شود. بنابراین، تغییرات چشمگیری ممکن است در اسکلت مادر رخ دهد. این مطالعه برای ارزیابی تغییرات مارکرهای خونی و ادراری استخوان سازی و جذب استخوان درحین حاملگی انجام شد.

روش کار: این مطالعه مورد شاهدی از مهرماه ۱۳۸٤- مرداد ۱۳۸۵ بر ۳۰۷ زن حامله در بیمارستان امام رضا (ع) مشهد انجام شد. کلسیم، فسفر، آلکالن فسفاتاز و ترشح ادراری ۲٤ ساعته کلسیم و فسفر در پرسشنامه جمع آوری گردید. اطلاعات با استفاده از نرم ا فزار SPSS 9.5، آنوا و توکیHSD تحلیل شد.

نتایج: آزمون آنوا نشان داد که تفاوت چشمگیری بین عوامل وابسته (کلسیم، فسفر، آلکالن فسفاتاز، ترشح ادراری ۲٤ ساعته کلسیم و سن مادر نبود (p=۰/۰۵۷)، اما ارتباط معناداری بین آلکالن فسفاتاز سرم، ترشح ادراری ۲٤ ساعته فسفر و مراحل مختلف حاملگی دیده شد (p=۰/۰۰۷). سطح سرمی آلکالن فسفاتاز در سه ماهه سوم، در مقایسه با سه ماهه های اول و دوم، متغیر بود. بهر حال، هیچ تفاوتی در این مقادیر در سه ماهه های اول و دوم دیده نشد.

نتیجه گیری: تغییر چشمگیری درمقادیر متوسط سطوح کلسیم و فسفر سرمی و ترشح ادراری ۲٤ ساعته کلسیم در سه ماهه های مختلف حاملگی دیده نشد (p= ۰/۰۷۰ و p=۰/۰۲۵ به ترتیب). همچنین، تغییرات در سطح سرمی متوسط کلسیم، ترشح ادراری ۲٤ ساعته فسفر در بیماران چندزا و نخست زا کاملا مشخص بود.

کلمات کلیدی: سه ماهه حاملگی، آلکالن فسفاتاز، کلسیم، فسفر

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Introduction

Fetus skeleton is formed during the pregnancy period and bone mineralization highly demands minerals, supplied maternally.

Science bone is the greatest reservoir for calcium, significant changes may occur in maternal skeletal system during the pregnancy that may result in osteoporosis and osteomalacia.

Although of the major part of calcium is absorbed by the fetus in the third trimester of pregnancy, however maternal calcium homeostasis begins from the earliest time of pregnancy (1).

It is demonstrated that the regulation of calcium metabolism in pregnancy occurs without any increase in ALP Level (2).

Power, et al mentioned a small significant increase in the serum calcium level, in the late pregnancy and showed that the serum phosphorus level was the same for the pregnant and nonpregnant women (3).

Seely,et al showed that while the total serum calcium and albumin levels decreased parallel to each other, serum ionized calcium remained unchanged (4).

Kaur, et al demonstrated some decrease and an increase in bone turn over, in the first and third trimesters of pregnancy, respectively (5). Also, the bone turnover increased during the lactation (5).

There are limited studies examining the effects of pregnancy on bone turn-over markers in human, however the existing evidence suggests that the turn-over is low in the first half and increases towards the end of pregnancy (6).

Most investigations about the bone metabolism in pregnancy which demonstrate serum ossification and urinary markers of bone absorption, are full of misleading variations; these are hemodilutional effect on serum markers, no access to basic normal levels before pregnancy, increase of GFR and renal clearance, changing in renal excretion of creatinine, different sources for markers from placenta, uterus and fetus, the role of placenta clearance and no access to NPO samples (7).

As the parity and age may influence the bone metabolism in each trimester of pregnancy and because previous researches demonstrated controversial data, this study was performed to assess the metabolic changes of calcium, phosphor and alkaline phosphatase in each trimester of pregnancy and their relationship with ossification, by evaluating the serum and urinary metabolic markers.

Material and Methods

This descriptive study was carried out from October 2005 to July 2006, on 307 women in different trimesters of pregnancy, visited at the Obstetric and Gynecology Ward of Imam Reza Hospital, Mashad, Iran.

Independent factors were, the gestational age, age of mother, and the number of parities; dependent factors included serum level of calcium and phosphorous (mg/dl), serum level of alkaline phosphates (u/l), and 24 hours urinary excretion of calcium and phosphorous (mg), which each one was measured by a single reference laboratory.

Data collected by questionnaire, analyzed With SPSS 9.05 software and the correlation of dependent factors with the age of mother was evaluated by Anova test. More over the relationship between some of dependent variables, parity and gestational age was analyzed with Tukey HSD test.

Results

In this assessment, patients were <20 (7.5%), 20-30 (70.5%) and >30 (22%) years old. Also, 47% and 53% of them were nulliparous and multiparous, respectively.

From the total patients were, 30% in the first, 36.8% in the second, and 33.2% in the third trimester of their pregnancy.

Anova test did not indicate to any exact correlation between dependent variables factors and the age of mother (P= 0.057) (table 1).

Table1: Distribution of central markers of serum calcium, phosphorous, ALP, 24 hours urinary excretion of phosphorous and calcium in different age groups of pregnant women in this study. (M=Mean, N=Number, SD=Standard deviation, U. exc= Urinary excretion).

Age group	Serum calcium			Serum phosph.			ALP			24h. u.exc.of calcium			24h.u.exc.of Phosph.		
	M	N	SD	M	N	SD	M	N	SD	M	N	SD			
<20	9.10	23	0.422	3.65	23	0.734	138.00	23	89.15	188.0	2	45.25	618.2	2	483.6
20-30	8.80	217	0.680	3.71	217	0.721	125.77	213	79.48	176.2	136	78.35	443.8	136	191.4
>30	8.88	67	0.660	3.58	67	0.680	131.32	67	62.37	153.1	43	70.47	402.7	43	223.8
Total	8.84	307	0.663	3.68	307	0.713	127.92		76.66	170.9	181	76.66	436.0	181	202.8

Analysis of the relationship between dependent variables and gestational age, showed no significant changes in the mean ratio of serum calcium, phosphorous level and 24 hours urinary excretion of calcium in different trimesters of pregnancy (P=0.070). However, the mean amount of serum ALP, 24 hours urinary excretion of phosphorous and the different trimesters of pregnancy were significantly correlated (P=0.07, P= 0.025).

The mean level of serum ALP in the third trimester, considerably varied from that for the first and the second trimesters; though, such varies could not be observed in the first and the second trimesters.

There was a reduction in the mean value for 24 hours urinary excretion of phosphorous in the third trimester, compared to the first trimester of pregnancy, although the same mean value did neither differ between the first and second nor between the second and third trimester (table 2).

Table2: Distribution of central markers of serum calcium, phosphorous, ALP, 24 hour urinary excretion of phosphorous and calcium in different trimesters of pregnant women in this study. (M=Mean, N=Number, SD=Standard deviation, U. exc= Urinary excretion, t= trimester).

Pregnancy Trimester	Serum calcium			Serum phosph.			ALP			24h. u.exc.of calcium			24h.u.exc.of Phosph.		
	M	N	SD	M	N	SD	M	N	SD	M	N	SD			
First t.	8.7	92	0.668	3.65	92	0.659	97.52	90	39.77	186.7	42	93.11	507.2	42	197.5
Second t.	8.85	113	0.630	3.61	113	0.656	104.39	111	46.81	171.3	62	68.54	423.8	62	148.1
Third t.	8.89	102	0.695	3.79	102	0.809	180.36	102	97.90	162.2	79	72.60	407.0	77	234.0
Total	8.84	307	0.663	3..68	307	0.713	127.92	303	76.66	170.9	183	76.76	436.0	183	202.8

Remarkable differences were seen in the mean level of serum calcium, 24 hours urinary excretion of Phosphorous in nulliparous and multiparous patients.

The mean level of serum ALP in the multiparous group was significantly less than the nuliparous group, and also, the 24 hours urinary excretion of phosphorous in the first group was less than that in the latter one (P= 0.000, P= 0.000, respectively) (Table 3).

Table3: Distribution of central markers of serum calcium, phosphorous, ALP, 24 hours urinary excretion of phosphorous and calcium in different parities in pregnant women in this study. (M=Mean, N=Number, SD=Standard deviation, U. exc= Urinary excretion, Grand M=Grand Multipare).

Parity	Serum calcium			Serum phosph.			ALP			24h. u.exc.of calcium			24h.u.exc.of Phosph.		
	M	N	SD	M	N	SD	M	N	SD	M	N	SD			
Nulipare	8.83	144	0.553	3.73	144	0.756	142.8	141	93.81	170.76	91	85.45	478.7	91	239.8
Multipare	8.80	143	0.763	3.64	143	0.678	115.9	142	56.09	170.56	87	68.15	393.7	86	149.1
Grand M.	9.13	20	0.597	3.55	20	0.663	107.6	20	45.77	180.20	5	56.29	373.0	4	51.47
Total	8.84	307	0.663	3.68	307	0.713	127.9		76.66	170.9	183	76.00	436.00	181	202.8

The result of General Linear Model Test, which was proceeded to evaluate the simultaneous effect of the three factors of pregnancy (gestational age, mothers' age and parity) on five dependent variables of this study, proved that both gestational age and parity, simultaneously affected the serum ALP level.

Discussion

The fetus needs nearly 30 gr calcium, 80% of which is achieved in the third trimester of pregnancy, and this amount is about 3% of the total maternal calcium (8).

Inspite of this achievement by the fetus in absorbing the major port of its calcium in the third trimester of pregnancy (200mg/day); maternal calcium homeostasis begins from the earliest time of this period (8,9). The fractional absorption ratio of calcium from GI doubles in the second trimester and remains at the same level until the end of pregnancy. The main reason for this alteration of absorption is increase of calcitriol due to the maternal renal hydroxylase or extrarenal sources of hydroxylase like fetus kidney or placenta (10).

The other factors like prolactine, growth hormone and estrogen can regulate calciteriol synthesis during pregnancy (2,10).

Regulation of calcium metabolism in this period occurs without any increase in ALP, and there is no change in calcium bioactivity which may be due to production of PTH related protein (PTHrp), produced in parathyroid glands of fetus and in placenta and increased during pregnancy (4).

Despite of decrease in total serum calcium in pregnant woman, due to physiologic hypoalbunemia, ionized serum calcium remains intact and dose not change (11, 12).

In the course of pregnancy 24 hours urinary excretion of calcium increases due to increase of GFR and returns to normal level after delivery (7,11).

Regarding the high prevalence of pregnancy in aged multiparous women in IRAN, This study was performed to assess the relationship between the metabolic, ossification changes, parity and the mother's age .

In pervious similar investigations, it has been demonstrated that bone absorption increases in the second and the third trimesters of pregnancy and the bone density decreases (3). In the present study, serum ALP level had significant difference in the third trimester compared to the first and the second trimesters, which demonstrated a sharp increase in the rate of bone metabolism.

Some investigators have described a decrease in bone density in ultrasonographic densitometry in the third trimester of pregnancy (3,14).

In this research, 24 hours urinary excretion of calcium was not correlated to the age of mother and the gestational age, but was more than the average in nonpregnant women.

Similar results have been reported at Missory University in Colombia (14). They

also have demonstrated that skeletal turnover markers had been higher in the third trimester and during lactation, but there was no increase in phosphatase resisted to tartarat and bone specific ALP. How ever in the present study, serum ALP level and mean 24 hours urinary excretion of phosphorus had significant difference in the third trimester match to the first and the second trimesters (14,15).

In the assessment of the effect of parity on serum and urinary metabolic markers the mean serum ALP and 24 hours urinary excretion of phosphorous were less in multiparous, compared with nulliparous group; no similar study was found to watch the results.

Conclusion

There was no significant alteration in the mean ratio of serum calcium, phosphorus level and 24 hours urinary excretion of calcium in different trimesters of pregnancy (P= 0.070).

There was remarkable correlation between the mean serum ALP, 24 hours urinary excretion of phosphorous and different trimesters of pregnancy (P= 0.007, P= 0.025 respectively).

Also, there was a clear difference in the mean serum calcium level, 24 hours urinary excretion of phosphorous in multiparous and nulliparous patients.

And finally, it is important to conclude that multiple pregnancies with short intervals may be a dangerous factor due to insufficient ossification and may cause early osteoporosis, osteomalacia, and bone fractures in the middle and late reproductive period.

Abstract

Introduction: Fetus skeleton is formed during pregnancy and calcium and phosphorous for this mineralization is provided by mother, so significant changes may occur in the mother's skeleton. This study was conducted to evaluate the changes of serum and urinary markers of ossification and bone absorption during pregnancy.

Material and Methods: In this cross-sectional study, from Oct. 2005 to Jul. 2006, 307 pregnant women, at Imam Reza Hospital in Mashhad, were randomly assessed. Serum calcium, phosphorous, ALP, 24 hours urinary excretion of calcium and phosphorus were determined. Data were analyzed by SPSS 9.5 software, ANOVA and Tukey HSD tests.

Results: ANOVA test indicated that, there was no significant difference between dependent variables (calcium, phosphorous, alkaline phosphatase), 24 hours urinary excretion of calcium, phosphorous and the age of mother (P=0.057), but there was meaningful relationship between serum ALP level, 24 hours urinary excretion of phosphorous and different trimesters of pregnancy (P=0.007). Serum ALP level in the third trimester was varied, compared to the first and second trimesters. However there was no difference in these amounts in the first and the second trimesters.

Conclusion: There was no significant alteration in the mean ratio of serum calcium, phosphorus level and 24 hours urinary excretion of calcium in different trimesters of pregnancy (P= 0.070). Noticeable correlation observed between mean serum ALP, 24 hours urinary excretion of phosphorous and different trimesters of pregnancy (P= 0.007, P= 0.025 respectively). Also, differences in the mean serum calcium level, 24 hours urinary excretion of phosphorous in multiparous and nulliparous patients was very clear.

Keywords: Trimester of Pregnancy, Alkaline Phosphatase (ALP), Calcium, Phosphorous

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