The Biochemical Changes in Bone Profile during Pregnancy

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ABSTRACT

Background: Metabolic processes directly affect the bone skeleton in the human body; especially during pregnancy in females. A bone profile obtained from a blood test can reveal the changes on it.
Objectives: The present study aims to estimate the changes that occur in some bone components during pregnancy and whether these changes are physiological or pathological.
Patients and methods: Blood samples were collected from 126 females who attend to Al-Hadbaa primary health care center and Al-Khansaa Hospital in Mosul city during the period from January to April 2008. These females classified into two main groups; Group-1 consists of 87 normal pregnant females which are subdivided to 3 subgroups according to their gestational age. Group-2 consists of 39 non-pregnant healthy females (control group). The biochemical parameters measured were: serum calcium, serum albumin, serum inorganic phosphorus (iP), serum alkaline phosphatase (ALP), and corrected serum calcium, and the measured data for these parameters were analyzed using different statistical methods.
Results: The total serum calcium, inorganic phosphorus and serum albumin decreased in pregnant female compared to the control group, while alkaline phosphatase activity was elevated in pregnant females compared to the non-pregnant females.
Conclusion: The increasing in ALP during pregnancy is accompanied by decreasing serum calcium in the 2nd trimester and decreasing in iP in the 3rd trimester that could be a pathological changes related to the bone.

Keywords: Bone profile, Pregnancy, Serum calcium, Inorganic phosphorus, Albumin, (ALP).

التغيرات الكيميائية الحياتية في مكونات العظم خلال الحمل

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الخلاصة

الخلفية: تؤثر عمليات التمثيل الغذائي بشكل مباشر على الهيكل العظمي في جسم الانسان وبخاصة عند فترة الحمل لدى النساء ويمكن من خلال مكونات العظم الذي يتم الحصول عليها من فحص الدم التعرف على التغيرات التي تحصل عليه.
الأهداف: هدفت الدراسة الحالية إلى تقدير التغييرات التي تحدث في بعض مكونات العظام أثناء الحمل وفي ما اذا كانت هذه التغيرات فسيولوجية أم مرضية.
طرق البحث: تم جمع عينات الدم ل ١٢٦ امرأة من مركز الحدباء للصحة الاولية ومستشفى الخنساء في مدينة الموصل خلال الفترة بين كانون الثاني الى نيسان ٢٠٠٨. قسمت العينات الى مجموعتين رئيسيتين. تتكون المجموعة الأولى من ٨٧ أمرأة حامل حملا طبيعيا وبدون مضاعفات مقسمة إلى ٣ مجموعات فرعية حسب مدة الحمل. تتكون المجموعة الثانية من ٣٩ من النساء الأصحاء غير الحوامل (مجموعة التحكم). كانت العناصر البيوكيميائية المقاسة هي: كالسيوم المصل ، ألبومين المصل ، الفسفور غير العضوي في الدم (iP) ، الفوسفاتيز القلوي في الدم (ALP), الكالسيوم المصحح و تم تحليل البيانات المقاسة لهذه العناصر باستخدام طرق احصائية مختلفة.
النتائج: بينت الدراسة ان هنالك انخفاض في إجمالي الكالسيوم والفوسفورغير العضوي في الدم وألبومين المصل في النساء الحوامل مقارنة بمجموعة التحكم ، بينما ارتفع نشاط الفوسفور القلوي للنساء الحوامل مقارنة بالنساء غير الحوامل.

الاستنتاجات: تترافق الزيادة في ALP أثناء الحمل مع انخفاض الكالسيوم في المصل في الثلث الثاني من الحمل وانخفاض في iP في الثلث الثالث من الحمل والذي يمكن أن يكون عبارة عن تغيرات مرضية متعلقة بالعظام.

الكلمات المفتاحية: مكونات العظم, الحمل, كالسيوم مصل الدم, الفوسفور اللاعضوي, الالبومين, الفوسفات القاعدي .

INTRODUCTION

Bone remodeling is mainly a local process carried out in small area by populations of cells called bone-remodeling cells. First, osteoclasts resorb bone, and then osteoblasts lay down new bone in the same area. In females, skeletal growth continues until approximately the age of 20, but bone mineralization may continue until the age of 35 [1].

Bone profile test consists of four main biochemical parameters including serum calcium, serum iP, serum albumin and serum ALP[2]. An average full-term fetus contains 30 gm calcium, and 20 gm phosphorus, and about 80% of mineral accreted during the third trimester of pregnancy[3], so maternal adaptation for this demand is important. Females who have sufficient calcium intakes of at least 1,000 mg per day at the start of pregnancy do not need for further calcium supplementation, but females with suboptimal intakes of less than 500 mg may be needed to satisfy both maternal and fetal bone requirements[4].

In general calcium homeostasis during pregnancy is a function of dietary intake, urinary excretion, and physiological hypoalbuminemia which is produced by hemodilution that occuring in pregnancy appears to be largely, if not completely, responsible for this condition[5]. Thus, the following formula is used to calculate the corrected calcium concentration[6]:

Corrected calcium (mmol/l) =measured total calcium (mmol/l) + 0.02 (40 – albumin (g/l))

Low levels of iP before pregnancy could result in its level depletion (hypophosphataemia) and subsequently leads to some of the diseases faced by females after pregnancy[7]. Serum ALP is primarily extracted from the liver and bones in more than 80 %[8], but in pregnancy during the second trimester, ALP activity becomes significantly higher than in the first trimester. This is primarily due to placental isoenzyme production and an increase in the bone isoenzyme, during the third trimester there is also an increase in the production of the bone isoenzyme as showed by an increase in its serum level of the six weeks post-delivery[9]. Osteomalacia is disorder in which mineralization of the organic matrix of the bone skeletal is defective which is due to the vitamin D deficiency. Vitamin D controls calcium and phosphate absorption and metabolism; it is obtained through the direct action of sunlight on the skin (90%) or through dietary nutrients (10%), in particular, dairy products, eggs and fish[10]. In the Middle East, vitamin D deficiency is common[11]. Recent researches further confirms that a state of vitamin D deficiency (VDD), also common among females during pregnancy[12], more than half of the mothers and their neonates had some degrees of vitamin D deficiency[13] particularly those of Asian origin[14]. For example in Iranian pregnant females prevalence of VDD and VD insufficiency was 76.7% and 14.6%, respectively[15]. Individual with darker skin is more susceptible to VDD, also osteomalacia occurred if a person with intestinal malabsorption and decrease exposure to sunlight[16].

The aims of this study were to estimating the changes that occur in some bone components during pregnancy, and try to diagnosing the cause of these changes whether physiological or pathological, in nature.

PATIENTS AND METHOODS

This study represents a case-control study. Eighty seven healthy pregnant females aged (14-42) years who attend to Al-Hadbaa primary health care center and Al-Khansaa Hospital as an outpatient. The control-group (non-pregnant females) includes thirty nine apparently healthy non-pregnant females aged (17-46) years. The females who had chronic diseases, or were taking medicines, or who had obstetric problems such as gestational diabetes, hypertensive disorder of pregnancy or premature delivery were excluded from the study. Oral consent was obtained from all females included in this study, and a complete history of both groups of females was obtained.

Determination of total calcium using colorimetric method[17], using a kit was supplied by biomerieux@SA (France). Determination of serum iP using a kit supplied by Biolabo (France). Method without deproteinisation was described by Daly and Ertingshausen[18]. Serum Albumin was determined using dye-binding method[19,20] using kit supplied from biomerieux@Sa (France). Colorimetric determination of serum ALP activity using a kit supplied by biomerieux@SA (France)[21]. Standard statistical methods were used for determination of the mean (x), Z-test is used to compare between pregnant females and the

control group, Unpaired (student's) t-test was used to compare between 1st, 2nd, and 3rd trimester each other and with the control group. Linear regression used to find the relationship between different parameters. All values quoted as the mean between observations were considered not significant at $p<0.05$[22]

RESULTS

During the comparison between the three trimesters of pregnancy flowing results are obtained: there is no significant (p>0.05) difference in serum calcium, serum albumin, and corrected calcium among the different trimesters of pregnancy, there is a significant ($p<0.005$) difference in serum inorganic phosphorus between 2nd trimester (0.97) mmol/l and 3rd trimester (0.83) mmol/l. ALP comparison shows a highly significant difference ($p<0.001$) between 1st trimester (5.07) K.A.U/100ml and 2nd trimester (8.88), also a significant difference ($p<0.015$) between 2nd trimester (8.88)K.A.U/100ml and 3rd trimester (11.91)K.A.U./100ml)),and a highly significant difference ($p<0.005$) between 1st and 3rd trimester as shown in table-1.

During the comparison between the pregnant and the control group, flowing results are seen: There is a highly significant decrease in serum albumin in pregnant females (35.09 g/L) compared to the control group (39.8 g/L). There is a highly significant ($p<0.001$) increase in the ALP activity level in pregnant females (9.07 K.A.U./100Ml) compared to the control group (6.05 K.A.U./100Ml).

Table-1: The differences between different parameters of bone profile for each trimester in pregnant females.

Parameter	Trimester	Mean ± SD	*P value
Total Ca (mmol/l)	1st 2nd	2.13 ± 0.23 2.1 ± 0.17	< 0.001
	2nd 3rd	2.1 ± 0.17 2.13 ± 0.19	< 0.015
	1st 3rd	2.13 ± 0.23 2.13 ± 0.19	< 0.001
Albumin (g/L)	1st 2nd	36.4 ± 12.5 35.17 ± 13.1	0.550 NS
	2nd 3rd	35.17 ± 13.1 34.16 ± 11.41	0.600 NS
	1st 3rd	36.4 ± 12.5 34.16 ± 11.41	0.300 NS
iP(mmol/l)	1st 2nd	0.91± 0.15 0.97 ± 0.08	0.390 NS
	2nd 3rd	0.97 ± 0.08 . 0.83 ± 0.08	< 0.005
	1st 3rd	0.91± 0.15 0.83 ± 0.08	0.170 NS
ALP K.A.U./100Ml	1st 2nd	9.07 ± 3.75 8.88 ± 3.71	< 0.001
	2nd 3rd	8.88 ± 3.71 11.91 ± 5.03	< 0.015
	1st 3rd	9.07 ± 3.75 11.91 ± 5.03	< ٠.٠٠١
Corrected Ca (mmol/l)	1st 2nd	2.35 ± 0.17 2.33 ± 0.26	0.840 NS
	2nd 3rd	2.33 ± 0.26 2.38 ± 0.30	0.410 NS
	1st 3rd	2.35 ± 0.17 2.38 ± 0.30	0.600 NS

* t-test

There is significant (p<0.007) reduction in the level of serum calcium in pregnant females and a significant decrease in the level of iP ,but no significant difference in corrected calcium is seen as in table-2. During the comparison between the pregnant females in the 1st trimester and the

control group, flowing results are seen: there is no significant difference in serum calcium, corrected serum calcium, ALP, iP, but just significant difference (p <*0,014*) in serum albumin between 1st trimester (36.8) g/l and (39.8) g/l in the control group as in table -3.

Table-2: Comparison between different parameters of bone profile between the control group and pregnant females.

Parameters	The control group (n = 39) Mean ± SD (Range)	Pregnant Group(n = 87) Mean ± SD (Range)	*P value
Total Ca (mmol/l)	2.22 ± 0.18 (1.88 - 2.70)	2.11 ± 0.23 (1.88 - 2.72)	< 0.007
Albumin(g/L)	39.8 ± 5.06 (32 - 50.2)	35.09 ± 11.22 (21.45 - 53.95)	< 0.001
iP (mmol/l)	1.02 ± 0.09 (0.64 - 1.45)	0.91 ± 0.11 (0.64 - 1.58)	< 0.010
ALP (K.A.U./100ml)	6.05 ± 2.60 (3.3 - 10.3)	9.07 ± 3.75 (3.51 - 25.80)	< 0.001
Corrected Ca.(mmol/l)	2.36 ± 0.21 (1.98 - 2.84)	2.35 ± 0.28 (1.78 - 3.00)	0.82 NS

* z-test

Table-3: Comparison between different parameters of bone profile in the control group and pregnant females in the 1st trimester.

Parameters	The control group Mean ± SD (n = 39)	First trimester Mean ± SD (n = 17)	*P value
Total Ca (mmol/l)	2.22 ± 0.18	2.13 ± 0.23	0.131 NS
Albumin (g/L)	39.8 ± 5.06	36.4 ± 12.5	< 0.014
iP (mmol/l)	1.02 ± 0.09	0.91± 0.15	0 .054 NS
ALP (K.A.U./100ml)	6.05 ± 2.60	5.07 ± 1.24	0.060 NS
Corrected Ca. (mmol/l)	2.36 ± 0.21	2.35 ± 0.17	0.791 NS

* t-test

The comparison between the pregnant females in the 2nd trimester and the control group shows the following results: There is a just significant elevation in of ALP activity in the serum of pregnant females (8.88 K.A.U./L) in comparison to the control group females (6.05 K.A.U./mL). There is a highly significant (p<0.001) reduction in the level of serum albumin in the pregnant females (35.17 g/L) in compared to the control group (39.8 g/L). There is a just significant (p<0.05) reduction in the level of serum calcium in pregnant females (2.1 mmol/l) compared to the control group (2.22 mmol/l) ,no significant difference in iP or corrected calcium is seen between the two groups as in (Table 4).

Table-4: Comparison between different parameters of bone profile between the control group and pregnant females in the 2nd trimester.

Parameters	The control group Mean ± SD (n = 39)	2nd trimester Mean ± SD (n = 17)	*P value
Total Ca (mmol/l)	2.22 ± 0.18	2.1 ± 0.17	< 0.008
Albumin (g/L)	39.8 ± 5.06	35.17 ± 13.1	< 0.001
iP (mmol/l)	1.02 ± 0.09	0.97 ± 0.08	0.283 NS
ALP (K.A.U./100ml)	6.05 ± 2.60	8.88 ± 3.71	< 0.001
Corrected Ca. (mmol/l)	2.36 ± 0.21	2.33 ± 0.26	0.560 NS

* t-test

During the comparison between the pregnant females in the 3rd trimester and the control group, flowing results are seen:

There is highly significant (p<0.001) elevation in ALP activity in pregnant females (11.91) K.A.U./100ml compared to the control group (6.05) K.A.U./100ml, a highly significant (p<0.001) decrease in serum phosphorus in pregnant females (0.83) compared to the control group(1.02) (mmol/l), and a significant (p<0.002) decrease in serum albumin in pregnant females (34.16)g/L compared to the control group(39.80)g/L no significant difference in s. calcium and corrected calcium between the two groups is seen (Table-5).

Figure-1 shows just significant (p<0.05) inversed relationship between corrected serum calcium and the ALP during pregnancy and this inversed relationship mostly obvious during 2nd trimester (Figure-2). When the correlation became highly significant (p < 0.001)

Table-5: Comparison between different parameters of bone profile and product between the control group and pregnant females in the 3rd trimester.

Parameters	The control group Mean ± SD (n = 39)	3rd trimester Mean ± SD (n = 17)	*P value
Total Ca (mmol/l)	2.22 ± 0.18	2.13 ± 0.19	0.075 NS
Albumin (g/L)	39.8 ± 5.06	34.16 ± 11.41	< 0.002
iP (mmol/l)	1.02 ± 0.09	0.83 ± 0.08	< 0.001
ALP (K.A.U./100ml)	6.05 ± 2.60	11.91 ± 5.03	< 0.001
Corrected Ca. (mmol/l)	2.36 ± 0.21	2.38 ± 0.30	0.670 NS

* t-test

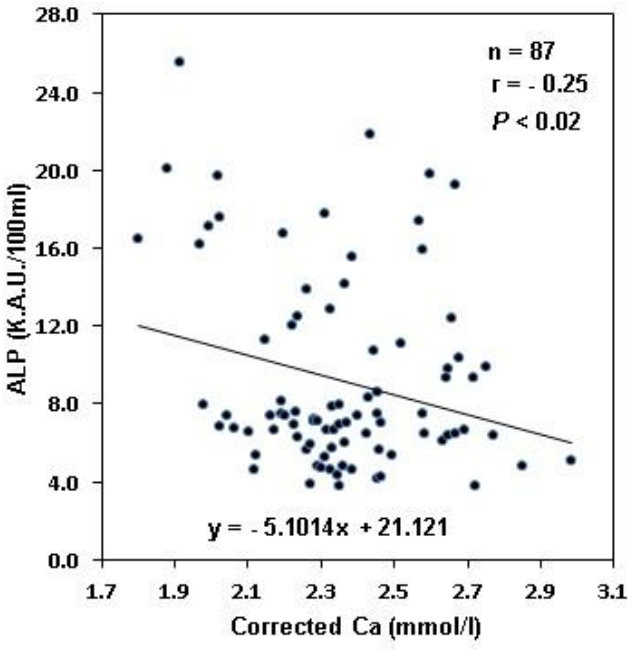

Figure-1: The relationship between corrected serum calcium (measured calcium (mmol/l) + 0.02[40 – albumin (g/l)]) and ALP during pregnancy

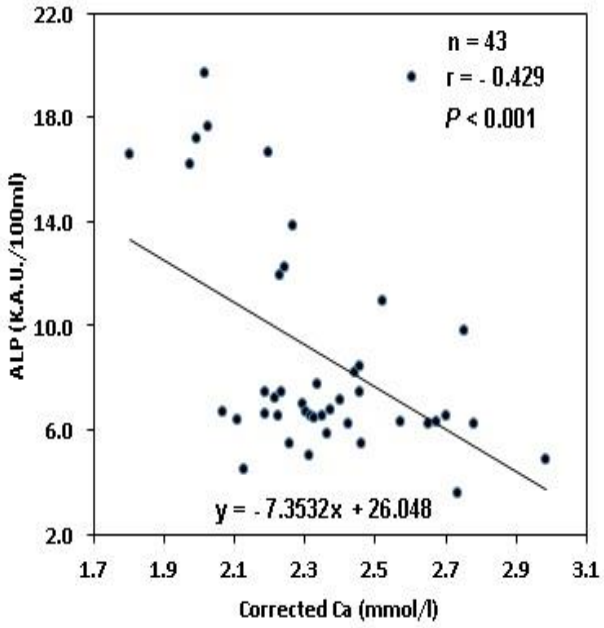

Figure-2: The relationship between corrected serum calcium and ALP during 2nd trimester of pregnancy

DISCUSSION

Hypocalcaemia in late pregnancy is highly prevalent (59%) among females in reproductive period[23]. In the present study serum calcium was tend to decrease throughout pregnancy, and the difference was just significant compared to the control group, especially in the 2nd trimester compared to the control group. The conclusion of this study was similar to a study was done in the west of Iran, in which (26.4 %) of pregnant females found to be hypocalcaemic[24], other report found that maternal serum calcium does not vary with increase in the gestational age, and that there is an increase in serum calcium in pregnant females compared to the non-pregnant controls but this report was done in a developed country[25]. Serum albumin shows no significant difference among different time of pregnancy, but a highly significant difference when compare serum albumin in pregnant females to the control group when (p<0.001), this result is in agreement with the study that found a marked decrease in serum albumin and this decrease is more in those who gestational age less than 37 wks. This is in contrary to the fact that serum albumin will decrease as the pregnancy progresses due to the dilutional effect of increase maternal plasma volume over increase total serum albumin during pregnancy[26], moreover this is in agree with another study done on Sudanese pregnant females that showed significant decrease in serum albumin during pregnancy[27].

Regarding serum iP the difference between the pregnant group and the control group was significant and the much affection appears obviously through the last trimester when the difference between 3rd trimester and the control group (p< 0.001). The same result obtained in a study done on Saudi pregnant females showed that iP decreased in pregnancy[5]. In Nigerian study serum iP differences was very highly significant between control and pregnant and between the three trimesters with each other[23]. These results support that the maternal urinary execration of iP levels increased during the third trimester of pregnancy[28].

Serum ALP activity shows highly significant difference (p<0.001) when compare it in the different trimester and with both 2nd and 3rd trimesters compared to the control group value, this because in pregnant females, the activity of the placental isoenzyme of ALP is increased. In the last trimester, the increase may be up to 4 times than the normal values[29,30].

Although the corrected calcium showed insignificant difference in this result there was an inversely correlation between serum ALP and corrected serum calcium (Figure-1). This inversed correlation was seen also during the 2nd trimester (Figure-2). This inversed correlation is parallel to the hypocalcaemia that seen during pregnancy especially in the 2nd trimester. This means that although apparently insignificant changes in corrected calcium but there is a tendency of ALP to increase.

CONCLUSIONS

The current study explained that the hypoalbuminaemia due to dilutional effect of pregnancy start early from 1st trimester. ALP increases during pregnancy accompanied by calcium decreasing in the 2nd trimester, while in the 3rd trimester ALP increasing is accompanied by iP decreasing.

The increasing ALP in pregnancy is not always considered as normal physiological changes explained by placental isoenzyme, but if it is accompanied by decreasing level of other elements of bone profile osteomalacia should not be forgotten.

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