Study of Parathyroid gland function in normal pregnant women in Tikrit city

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Abstract:

Background: During pregnancy, there an increase in calcium demands to helps building of fetus's skeleton, to met this demands the parathyroid gland secretes parathyroid hormone to maintain calcium homeostasis. ***Aim of study****:* is determine the function of parathyroid gland and calcium turnover during pregnancy in normal healthy pregnant women in Tikrit city. ***Subjects and methods:*** A longitudinal follow up study was conducted in Ibn-Rushed health care center at Tikrit city. The study was done from the 15th of November 2016 to the end of March 2017. Thirty healthy pregnant women was participated in the present study, aged from 18 to 40 years in their 15–18th week of pregnancy. All pregnant women were followed up every month, about 5 ml of venous blood was drawn from the pregnant women every four weeks till the end of the 2nd trimester or the beginning of 3rd trimester. The blood lifted to clotted then centrifuged to separate the serum. The separated serum kept in deep freezing, until collection of all samples to be used in hormone and biochemical analysis. ***Results:*** PCV and Hb shows a highly-significant difference ($P \leq 0.01$) among these three followed-up months. There is a highly-significant difference ($P \leq 0.01$) in serum PTH in the three followed-up months. Prolactin concentrations were significantly higher during the second trimester, in other hand there is no-significant difference in serum osteocalcin concentration between the first trimester as compare with the second trimester ($P > 0.05$). Serum calcium and phosphors shows a no-significant difference ($P > 0.05$) in the three followed-up month of 30 pregnant women. Magnesium shows a significant difference ($P \leq 0.05$) in the results of the three-follow-up month, while in ALP there is a highly-significant difference ($P \leq 0.01$) in the results, the highest value in the 5th month.

Key word: Pregnancy, First and second trimester, Parathyroid hormone, Calcium, Alkaline phosphates.

دراسة وظيفة الغدة جنب الدرقية في النساء الحوامل في مدينة تكريت

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الخلاصة:

خلال فترة الحمل، وهناك زيادة في احتياج الكالسيوم للمساعدة في بناء الهيكل العظمي للجنين، لتلبية هذا الاحتياج الغدة جنب الدرقية تفرز هرمون الغدة جنب الدرقية للحفاظ على التوازن الكالسيوم. الهدف من الدراسة: هو تحديد وظيفة الغدة الدرقية ودوران الكالسيوم أثناء الحمل في النساء الحوامل الأصحاء الطبيعيات في مدينة تكريت. الأشخاص والطرائق العمل: أجريت دراسة متابعة طولية في مركز ابن رشد للرعاية الصحية بمدينة تكريت. أجريت الدراسة من 15 نوفمبر2016 حتى نهاية مارس 2017. وقد شاركت ثلاثين امرأة حامل صحية في هذه الدراسة، اللاتي تتراوح أعمارهن بين 18 و40 عاما في الأسبوع 15- 18 من الحمل. تمت متابعة جميع النساء الحوامل كل شهر، حيث تم سحب حوالي 5 مل من الدم الوريدي من النساء الحوامل كل أربعة أسابيع حتى نهاية الثلث الثاني من الحمل أو بداية الثلث الثالث من الحمل. الدم يوضع في جهاز الطرد المركزي لفصل المصل. المصل فصل وتم الاحتفاظ به في تجميد عميق، حتى جمع جميع العينات لاستخدامها في التحليل الهرموني والكيمياء الحيوية. ***النتائج:*** حجم كريات الدم المضغوطة والهيموكلوبين يظهر فرق كبير جدا ($P \leq 0.01$) بين هذه الأشهر الثلاثة المتابعة. هناك فرق كبير جدا ($P \leq 0.01$) في هرمون الغدة جنب الدرقية في المصل في الأشهر الثلاثة. كانت تراكيز البرولاكتين أعلى بكثير خلال الثلث الثاني من الحمل، ومن ناحية أخرى لا يوجد فرق معنوي في تركيز أوستيوكلاسين المصل بين الثلث الأول من الحمل مقارنة مع الثلث الثاني ($P< 0.05$)

يظهر الكالسيوم والفسفور في مصل الدم فرقا غيرمعنوي ($P< 0.05$) في الشهر الثالث من المتابعة. يظهر المغنيسيوم فرقا معنويا ($P \leq 0.05$) في نتائج الشهر الثالث للمتابعة، بينما في ALP هناك فرق كبير جدا ($P \leq 0.01$) في النتائج، وهي أعلى قيمة في الشهر الخامس.

الكلمات المفتاحية: الحمل، الثلث الاول و الثاني، هرمون جنب الدرقية و الكالسيوم

Introduction:

The requirement of calcium for the growing fetus is about 30 gm of calcium to complete mineralization of its skeleton system and insure proper physiological process. This requirement generally induces alterations in maternal homeostasis of calcium to allow active transport throughout placenta. [1]

There are several factors that known to be involved in balanced relationship between the large pool of calcium in skeleton and the much smaller pool of extra cellular fluid, one of the important factors that maintain the calcium and other related minerals balance such as magnesium and phosphate are hormones such as parathyroid hormone (PTH). [2]

PTH acts mainly on three tissues which are bone, kidney and intestine, this hormone raises blood calcium level (hyper calcium effect). PTH stimulate calcium reabsorbtion in kidney and also enhance hydroxylation of 25-Hydroxy vitamin D3 which responsible for increasing calcium uptake by small intestine. Finally in bone, PTH stimulates bone resorption of serum calcium, this process increase in pregnancy to met the large demand for calcium.[3]

So PTH levels are inversely related to calcium concentration in blood, increasing PTH when there is an increasing in calcium level, acting through PTH receptor which is highly in bone and kidney. The increases are evident by early to mid pregnancy for calcium by growing skeleton of the fetus. In addition releasing of PTH controlled by plasma phosphorus and magnesium levels, any elevation in plasma phosphorus levels increase PTH secretion.[4,5]

Aim of study:

Is to determine the function of parathyroid gland and calcium turnover during pregnancy in normal healthy pregnant women in Tikrit city.

Subjects and methods:

A longitudinal follow up study was conducted in Ibn-Rushed health care center at Tikrit city. The study was done from the 15th of November 2016 to the end of March 2017. Thirty healthy pregnant women was participated in the present study, aged from 18 to 40 years in their 15–18th week of pregnancy. All pregnant women were followed up every month, about 5 ml of venous blood was drawn from the pregnant women every four weeks till the end of the 2nd trimester or the beginning of 3rd trimester. The blood lifted to clotted then centrifuged to separate the serum. The separated serum kept in deep freezing, until collection of all samples to be used in hormone and biochemical analysis. All data were presented as Mean and Stander deviation (SD). F test (One way, ANOVA) was used to compare between means of variables. P value less than 0.05 or 0.01 was used as significant value.

Results:

Regarding PCV there is a highly-significant difference ($P \leq 0.01$) among these three followed-up months, the 3rd month of pregnancy **36.200 ±2.295 %** as compare with the 4th month 34.733 **±2.212** and the 5th month **33.333 ± 2.294.** As the same as in Hb, there is a highly-significant difference ($P \leq 0.01$) among these three followed-up months, the 3rd month of pregnancy shows the highest value **11.777 ±0.910 gm/dl** as compare with the 4th month **11.050 ±0.785 gm/dl** and the 5th month

10.643 ±0.849 gm/dl, as shown in table (1).

There is a highly-significant difference **(P ≤ 0.01)** in serum PTH in the three followed-up months, the 5th month shows the highest value **40.73 ±2.78 pg/mL** as compare with the 4th month **25.88 ±1.73 pg/mL** and the 3rd month **19.41 ±2.16 pg/mL**, as shown in table2. Prolactin concentrations were significantly higher during the second trimester **6464 ± 439 pg/mL** as compared with first trimester **1920 ± 389 pg/mL (P ≤ 0.01).** There is no-significant difference in serum osteocalcin concentration between the first trimester **15.63 ± 6.54 ng/ml** as compare with the second trimester **16.229 ± 4.7 ng/ml (P > 0.05),** as shown in table (3).

Serum calcium and phosphors shows a no-significant difference **(P > 0.05)** in the three followed-up month of 30 pregnant women. Magnesium shows a significant difference **(P ≤ 0.05)** in the results of the three-follow-up month. The 4th month shows the lowest value **1.9000 ± 0.1287** as compare with 5th month **1.9733±0.1230** and 6th month **1.9833 ± 0.1234,** while in ALP there is a highly-significant difference (P ≤ 0.01) in the results, the highest value in the 5th month **170.97 ± 44.03** µkat/L as compare with 4th month **134.23 ± 28.14** µkat/L and 3rd month **116.37 ± 31.21** µkat/L, as shown in table (4).

Discussion:

In this study there was an anemia in pregnancy due to iron and vitamin B_{12} deficiency which is most cause of anemia in pregnant women, because iron supplementation programs are ineffective programs. Other nutritional deficiencies and inflammatory or infectious disease also cause anemia. (6)

In the present study, there is a highly significant increase ($P \leq 0.01$) in the concentration in Parathyroid hormone due to significant changes that combine pregnancy changes in all chemical parameters and hormones, including the sex steroids, prolactin, placental lactogen, and insulin-like growth factor type 1, all of these could have direct or indirect effects on calcium and bone metabolism during pregnancy. (7)

Decreasing in total serum calcium and rising in parathyroid hormone may cause secondary hyperparathyroidism in pregnancy, this is a rare condition. (8)

There was a profound increasing in Parathyroid hormone during 2nd trimester of pregnancy, which is indicate the elevated calcium demined by maternal and fetus. This demined may stimulates PTH release due to changes in calcium-sensing receptor (CaR) sensitivity of the parathyroid gland during pregnancy. (9)

Maternal calcium absorption mediated through increases in PTH synthesis rises during pregnancy to meet these demands. Paralleling a decline in serum albumin, total serum calcium concentrations decline during gestation, with little change in ionized calcium. In response to placental calcium transfer as well as an expanding extracellular volume and increased urinary calcium loss, maternal PTH concentrations rise during pregnancy. (10)

Prolactin increase during pregnancy and activate prolactin receptors. Prolactin concentrations may increase throughout the course of pregnancy, reaching a maximum at the end of pregnancy, due to changes in serum PTHrP during the course of pregnancy, the pregnancy stimulate increase in calcitropic hormone concentration, which may lead to

primary mediator of the changes in maternal calcium metabolism, but the involvement of other factors cannot be excluded. [11]

Osteocalcin consider as a bone-specific protein which released into circulation due to increasing in the rate of new bone formation. We founded that serum osteocalcin concentrations were moderately increased at the second trimester. Such changes are consistent with the expected changes in maternal bone turnover during the course of pregnancy: bone turnover is in limited levels during early pregnancy, in the second trimester bone turnover started to elevated until it reaches the highest level in third trimester. Other study disagrees with our results. [12]

Calcium fractional absorption ratio may lead to normal levels of calcium concentration from GI which is duplicates 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. [11]

The expanded intravascular space during pregnancy may cause serum total calcium, phosphate and magnesium tend to be low. In addition, calcium concentrations may also have affected by the reduced albumin concentration. However, results all remain within the reference range. [13]

In pregnancy there are high alteration in ca homeostasis due to the increasing demands of calcium during pregnancy and lactation. In late of gestation 2–3% of maternal Ca is transferred to the fetus to meet the high demands of calcium, also during pregnancy there are an

increase in absorption of intestine and bone turnover. (14)

The P and Mg levels conceder as an additional regulatory control of PTH releasing, decrease in the formation of arachidonic acid and activity of phospholipase are the ways to increase PTH secretion in case of plasma phosphorus levels is elevated so the inhibition effect of PTH secretion is removed. Elevations in P levels can also affect PTH release indirectly by decreasing plasma Ca^{+2} levels and vitamin D activation. (15)

The concentration of magnesium in the serum plays consider as a key role in PTH regulation, a moderate decrease in magnesium levels may stimulates a paradoxical block in PTH release. In addition, any decrease in magnesium levels may cause hypertension in pregnancy. (16)

Magnesium plays an important role during pregnancy, pregnant women tend to have low blood magnesium level than non pregnant because of increase demand for mother due to growing fetus and increase renal excretion, the loss of magnesium in pregnant women 25% higher than non-pregnant women due to increase in GFR and haemodilution in 2nd and 3rd trimester. (17)

In the present study, serum ALP level had a highly significant increased in second trimester compared to the first trimesters, which may show an increase in the metabolism of bones, in other studies the researchers had described this status as loss in bone density. (18)

In pregnancy the most important parameters are ALP and calcium, which undergo a high alteration in homeostasis hormones that may have effect on these parameters in pregnant women, as well as calcium related to the building of fetus body. (19) This increase in serum ALP levels in

progressing of pregnancy may indicate bone problems due to an increase in calcium demands as a results of new bone formation (fetus growing). [20]

The physiological alterations of pregnancy considered as adaptation that occur normally in maternal body to insure better accommodation of embryo or fetus during pregnancy. Calcium, the most abundant mineral in the human body, has several important functions. The significant increasing of total alkaline phosphatase (TAP) suppose there is a mainly stimulation caused by bone origin. [21]

This study concludes there was profound increase in PTH secretion during the second trimester as compare with first trimester.

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Table (1) PCV and Hb differences during the three follow-up months of pregnancy:

Parameters / Subjects	PCV %	Hb gm/dl
3rd month	**36.200 ±2.295 a**	**11.777 ±0.910 a**
4th month	**34.733 ±2.212 b**	**11.050 ±0.785 b**
5th month	**33.333 ±2.294 c**	**10.643 ±0.849 c**
P-Value	**0.0002**	**0.0003**

Table (2) PTH differences during the three follow-up months of pregnancy:

Parameters / Subjects	PTH(pg/mL)
3rd month	19.41 ±2.16
4th month	25.88 ±1.73
5th month	40.73 ±2.78
P-value	0.0001

Table (3) Prolactin and osteoclacin differences during first and second trimester:

Parameters / Subjects	Prolactin (pg/mL)	Osteoclacin (ng/ml)
First trimester	1920 ± 389	15.630 ± 6.54
Second trimester	6464 ± 439	16.229 ± 4.70
P-value	P ≤ 0.01	P ≤ 0.05

Table (4) Biochemical parameters differences during the three follow-up months of pregnancy:

Parameters / Subjects	Calcium levels (mg/dL)	Phosphors levels (mg/dL)	Magnesium levels (mg/dl)	Alkaline Phosphates (µkat/L)
3rd month	8.7600 ±0.4256	3.8703 ±0.2136	1.9000 ± 0.1287	116.37 ±31.21
4th month	8.5670 ±0.6950	3.8741 ±0.2118	1.9733 ± 0.1230	134.23 ±28.14
5th month	8.6733 ±0.5139	3.8221 ± 0.2025	1.9833 ± 0.1234	170.97 ±44.03
P-Value	0.407	0.575	0.05	0.001