

Bone ultrasonometry measurements during pregnancy

Monica Della Martina · Anna Biasioli · Lisa Vascotto · Davide Rinuncini ·
Arianna Adorati Menegato · Sara Liva · Ambrogio Pietro Londero ·
Lorenza Driul · Diego Marchesoni

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Abstract

Purpose During pregnancy we can have changes of the calcium metabolism that can determine a loss of bone mass. Some studies used single-photon absorptiometry (SPA) or dual-energy X-ray absorptiometry, but these exams are inadvisable in pregnancy for the teratogenic effects on the fetus. We used quantitative ultrasonometry (QUS). The aim of this study is to determine prospective changes of bone density with an ultrasonometry measurement during pregnancy in healthy Italian women.

Methods The study population was represented by 59 pregnant women. Quantitative ultrasonometry measurements were performed at the phalanges during the first, second and third trimester.

Results We found a progressive decrease of bone time transmission (BTT) from the first to the third trimester, while amplitude dependent speed of sound (AD-SoS) remained stable between the first and the second trimester and decreased at the term of pregnancy. The *z*- and *t*-scores decreased more during the second and third trimester.

Conclusions These results show an important reduction in the third trimester of pregnancy, of all ultrasonometry variables and then an increase of remodelling with bone

demineralisation in the mother. These results show that there is a different bone metabolism in pregnancy in pluriparous and nulliparous women.

Keywords Bone · Pregnancy · Ultrasonometry · Calcium metabolism

Purpose

Calcium is an essential element during pregnancy and lactation. During gestation, about 20–30 g of calcium is conferred to the foetus through the placenta [1]. More specifically, throughout pregnancy, the foetus transitions from requiring 2 to 3 mg of calcium per day, in the first trimester, to requiring 250 mg day⁻¹ near the end of pregnancy [2]. Pregnancy-induced changes in the metabolism of calcium may lead to the loss of bone mass in the mother, although the mechanisms by which this occurs are not fully understood.

Previous research studying bone loss in pregnancy has been done using single-photon absorptiometry (SPA) or dual-energy X-ray absorptiometry (DEXA); however, the results from these studies are conflicting. In addition, the techniques used in these studies are inadvisable in pregnancy due to the teratogenic effects on the foetus [3–6].

Quantitative ultrasonometry (QUS), a novel technology, offers researchers an inexpensive, radiation-free method by which to assess bone mineral density and bone quality. In addition, the ultrasound variables generated in QUS permit the prediction of hip and vertebral fractures in the same way that the DEXA scan does [7–17]. The aim of the present study is to use ultrasonometry measurements to determine prospectively bone density changes during pregnancy in a sample of healthy Italian women.

M. Della Martina · A. Biasioli (✉) · L. Vascotto · D. Rinuncini ·
A. Adorati Menegato · S. Liva · A. P. Londero · L. Driul ·
D. Marchesoni
Clinica di Ginecologia e Ostetricia,
Azienda Ospedaliero-Universitaria di Udine,
piazza S. Maria della Misericordia, Udine, Italy
e-mail: anna.biasioli@libero.it

Methods

Our sample consisted of 59 pregnant women, in the early stage of pregnancy, who presented to the Department of Obstetrics and Gynecology of Udine between February 2007 and September 2007 for obstetrical care. These women were between the ages of 24 and 39 and were included in the study if they came to the clinic to receive either their first ultrasound or their first nuchal translucency measurement.

Before entry into the study, all women signed a written consent to participate.

We recorded age, height, weight (at the beginning of the pregnancy and during the first, second, and third trimester), and body mass index (BMI) for each woman. We also recorded the date of the last menstrual period, the date of delivery, the number of children or abortions, the outcome of previous pregnancies, and lactation in previous pregnancies.

We also obtained data on whether women had taken hormone therapy before gestation, vitamins during pregnancy, medicines during or before pregnancy, or heparin during or before pregnancy.

All women answered a questionnaire on important risk factors for osteoporosis. The variables included on this survey are as follows: race, history of previous fractures, anorexia (BMI < 19), cigarette use (>10 cig day⁻¹), alcohol ingestion (>3 glasses of wine day⁻¹), coffee consumption (>3 day⁻¹), dietary calcium intake, physical activity level, age at menarche, periods of amenorrhea, use of drugs (i.e., corticosteroids, chemotherapy, heparin), history of thyroid disease, history of diabetes, history of kidney failure, and history of bowel diseases.

Quantitative ultrasonometry measurements were performed at the phalanges with the DMB Sonic 1200 (Igea, Italia). Values for the amplitude dependent speed of sound (AD-SoS), *t*-score, *z*-score, ultrasound bone profile index (UBPI), and bone time of transmission (BTT) were obtained.

The “amplitude dependent speed of sound” (AD-SoS; in m s⁻¹) is the speed of propagation of the ultrasound signal through the phalanx. In vitro and in vivo studies have demonstrated that AD-SoS is more strictly related to bone mass and bone density than to structure. Studies conducted on adults have indicated a strong correlation between AD-SoS and cortical bone thickness, an index of bone resistance.

The “ultrasound bone profile index” (UBPI; in units of probability) is an index derived from the analysis of an important database of measures that, through optimisation of the ability to discriminate between fractured and non-fractured subjects, provides an estimate of the probability that the subject will suffer an osteoporotic fracture. In vitro

studies have demonstrated that such an index is related to the structure and elasticity of bone tissue crossed by the ultrasound. The UBPI is calculated by a specific algorithm (signal processing technique) related to fracture risk [17] and is a value ranging from 0 (osteoporotic subject) to 1 (normal subject). The UBPI parameter is a useful means to quantify the structural and elastic properties of bone in our subjects.

The “bone transmission time” (BTT; in microseconds) is a parameter extracted from the graphic trace by means of the signal analysis. It is mathematically demonstrated that, unlike AD-SoS, the parameter does not depend on the thickness of the soft tissue surrounding the bone. For this reason, the BTT is a reasonable parameter to follow the effect of therapy on an individual patient.

The measurements were performed, by the same investigator, on pregnant women during the first trimester, namely, early pregnancy (between week 11 and week 15); the second trimester (between week 20 and week 25), and the third trimester (between week 32 and week 36 of gestation). Probes were positioned at the distal metaphysis of the first phalanx and adjacent to the condyles of the second through fourth digits.

At the beginning of the exam, we measured the reference speed of the patient’s soft tissue by applying the probes to the soft tissue area between the base of the thumb and the index finger.

Statistical analysis

Statistical analysis was performed with R a Language and Environment for Statistical Computing (Version 2.7.0). Distribution analysis showed that all variables fit the normal curve (Kolmogorov–Smirnov test). To evaluate the differences according to each trimester, the *t* test was used for paired samples.

Data were considered significant at *P* values <0.05.

Results

Table 1 shows the characteristics of our population.

The analyses of the variables (i.e., *z*-score, *t*-score, AD-SoS, BTT and UBPI) with the Kolmogorov–Smirnov test showed that all variables were normally distributed, with the exception of UBPI in the third trimester.

In order to evaluate bone density over the entire period of the pregnancy, we analysed the means of the variables obtained with ultrasonometry of the phalanges and the differences between the values calculated in each trimester for the population using the *t*-test for paired samples.

We then considered the number of previous pregnancies reported and divided the population into two groups,

Table 1 Characteristics of our population

	First trimester	Second trimester	Third trimester
GA (weeks) (SD)	13 (± 1.45)	22.71 (± 2.06)	35.45 (± 1.51)
BMI (SD)	23.37 (± 3.26)	25 (± 3.33)	26.94 (± 3.36)
Weight (kg) (SD)	65.13 (± 9.45)	69.81 (± 8.74)	75.15 (± 9)
z-Score (SD)	0.04 (± 0.9)	0.08 (± 0.85)	−0.39 (± 0.75)
t-Score (SD)	0.04 (± 0.91)	0.07 (± 0.84)	−0.4 (± 0.75)
AD-SoS (m s^{-1}) (SD)	2126.9 (± 63.83)	2128.07 (± 59.25)	2096.08 (± 53.21)
BTT (μs) (SD)	1.66 (± 0.17)	1.65 (± 0.15)	1.61 (± 0.16)
UBPI (SD)	0.75 (± 0.12)	0.78 (± 0.1)	0.77 (± 0.11)
Mean (standard deviation)			

Table 2 Variables (mean $\pm$ standard deviation) by groups

Variable		First trimester	Second trimester	<i>P</i> (mean of the differences between first and second)	Third trimester	<i>P</i> (mean of the differences between second and third)
AD-SOS (m s^{-1}) (SD)	All	2126.9 (± 63.8)	2128 (± 59.2)	0.940	2096 (± 53.2)	<0.05
	Nulliparous	2124.9 (± 66.4)	2117.9 (± 56)	0.260	2096.4 (± 56.8)	<0.05
	Multiparous	2130.4 (± 60.3)	2145.9 (± 61.8)	0.230	2095.5 (± 47.1)	<0.05
BTT (μs) (SD)	All	1.66 (± 0.15)	1.65 (± 0.16)	0.069	1.63 (± 0.21)	<0.05
	Nulliparous	1.65 (± 0.16)	1.62 (± 0.13)	<0.05	1.6 (± 0.15)	<0.05
	Multiparous	1.69 (± 0.19)	1.68 (± 0.18)	0.740	1.62 (± 0.19)	<0.05
UBPI(SD)	All	0.75 (± 0.12)	0.78 (± 0.10)	<0.05	0.77 (± 0.10)	<0.05
	Nulliparous	0.76 (± 0.13)	0.79 (± 0.1)	0.070	0.77 (± 0.1)	0.201
	Multiparous	0.74 (± 0.11)	0.78 (± 0.11)	<0.05	0.75 (± 0.12)	0.124
t-score	All	0.04 (± 0.9)	0.07 (± 0.84)	0.860	−0.4 (± 1.1)	<0.05
	Nulliparous	0.02 (± 0.96)	−0.09 (± 0.8)	0.250	−0.4 (± 0.8)	<0.05
	Multiparous	0.09 (± 0.85)	0.34 (± 0.87)	0.163	−0.39 (± 0.66)	<0.05
z-score	All	0.04 (± 0.92)	0.08 (± 0.92)	0.790	−0.39 (± 1.1)	<0.05
	Nulliparous	−0.003 (± 0.94)	−0.07 (± 0.8)	0.310	−0.39 (± 0.8)	<0.05
	Multiparous	0.11 (± 0.85)	0.12 (± 0.9)	0.172	−0.38 (± 0.66)	<0.05

nulliparous pregnant women ($n = 38$) and multiparous pregnant women ($n = 21$) (Table 2).

There was a statistically significant change in AD-SoS scores between the second and third trimester in every group; however, there were not significant differences between the first and second trimester (Fig. 1).

We observed a small increase in the values between the first and second trimester for our population and a significant decrease between the second and third trimester.

In the group of nulliparous pregnant women, there was a significant decrease in Ad-SOS during the pregnancy in particular between the second and the third trimester.

In the group of pluriparous pregnant women, Ad-SOS was lower at the beginning of pregnancy but increased between the first and second trimester and decreased between the second and third trimester.

The results for the BTT change in both the total sample and in the group of the nulliparous were statistically significant. In the total sample, BTT decreased significantly throughout pregnancy; we found a similar result in the

group of the nulliparous. There was not a significant reduction of BTT in the pluriparous group between the first and second trimester but there was a significant decrease between the second and third trimester (Fig. 2).

UBPI values changed significantly in all the groups except in the mean of the differences between the second and third trimester for women in the nulliparous and pluriparous groups.

All the values showed an increase between the first and second trimester and an important decrease between the second and third trimester.

In the pluriparous women, UBPI at the beginning of the pregnancy was lower than in nulliparous women and the decrease between the second and third trimester was larger for pluriparous women than nulliparous women.

Z-score and T-score values decreased significantly between the second and third trimester in all the groups, but there was not a significant change between the first and second trimester.

We found no significant influence of possible risk factors such as previous pregnancies or lactation on QUS

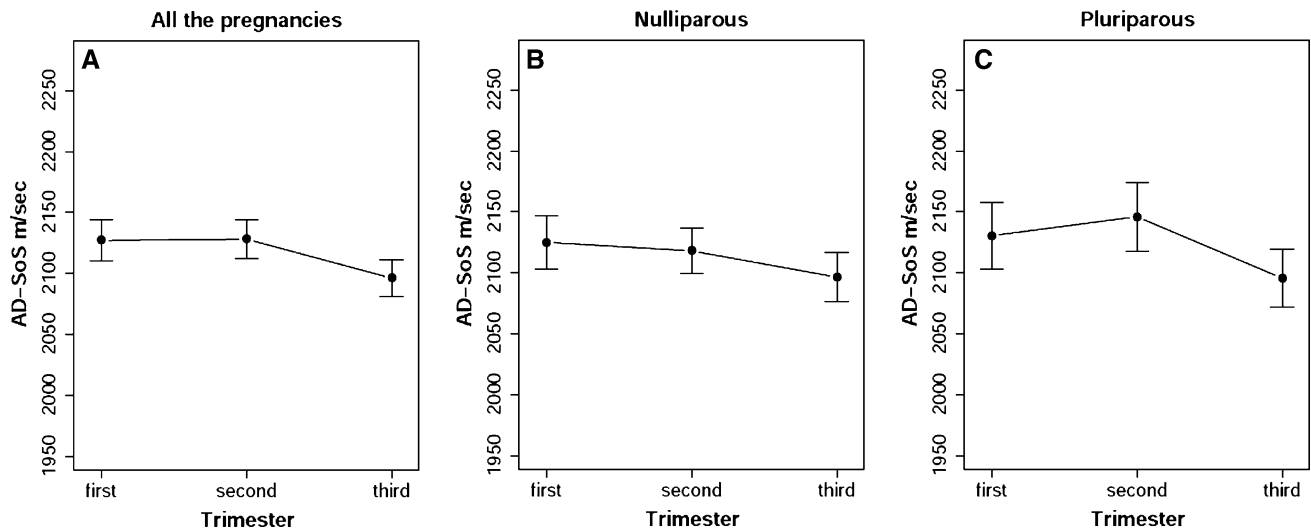


Fig. 1 AD-SoS changes during the pregnancy in all the pregnancy (a), nulliparous (b), and multiparous (c). I.C. 95% of mean

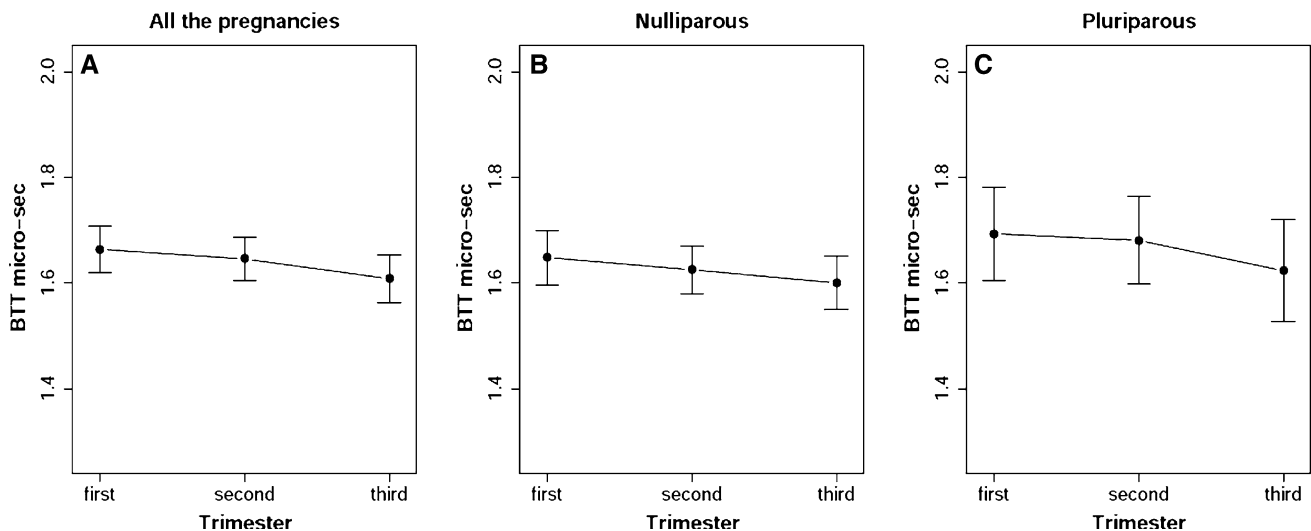


Fig. 2 BTT changes during the pregnancy in all the pregnancy (a), nulliparous (b), and multiparous (c). 95% CI of mean

measurement results. Among the 59 women, there were 21 multiparous women (35.59%). In the group of multiparous women, the average number of previous pregnancies was 1.29 (SD = 0.73–1.75); 18 of the 21 women breastfed (85.71%); the average number of months lactating was 8.48 (SD 2.57–14.38).

The only risk factor we observed that was statistically related to any measure of bone density was the number of previous pregnancies. The number of previous pregnancies was related to the change in AD-SoS, z -score, and t -score measurements in the second trimester of pregnancy.

We were unable to find a relationship between lactation during the previous pregnancies or lack of physical activity and QUS measurements results.

We next evaluated the consumption of vitamins during pregnancy. Of our sample, 47.76% took vitamins. However,

vitamin intake did not have a significant influence on QUS measurements results during any period of the pregnancy.

We also analysed the influence of increased BMI on QUS measurements. We found that BMI was a significant risk factor throughout the pregnancy and influenced all QUS measurement results with the exception of the BTT and UBPI.

Finally, we examined the variation (Δ) of BMI and the variation (Δ) of QUS measurements between the first and second trimester and between the second and third trimester.

We found that increases in BMI showed a significant influence during the first period (first to second trimester) on all QUS measures, except for the UBPI, while increases in BMI during the second period had no influence on any QUS parameters.

Conclusions

The effects of pregnancy on the maternal skeleton are largely discussed because of the correlation between the reduction of bone mineral density in a woman during pregnancy with demineralisation and perhaps pathologic long-term effects [2, 18].

The demand of calcium for foetal bone development may be regulated by a maternal compensatory mechanism [4]. This is to say that, during pregnancy, enormous demands for calcium are compensated for by an increase in intestinal absorption of calcium as well as an increase in the mobilisation of calcium from the maternal skeleton at the end of gestation.

Changes in bone mineral density during pregnancy have been studied for a long time, but have shown inconsistent results. Studies have evaluated decreases in bone density with plasmatic markers present during skeletal growth, urinary markers of renal absorption, and markers of bone remodelling [3–5, 19, 20].

Results showed an increase in urinary markers (i.e., deoxypyridinoline, pyridinoline and hydroxyproline) and a decrease in plasmatic markers (i.e., osteocalcin, procollagen I, carboxypeptidase and alkaline phosphatase) during the first half of pregnancy. Plasmatic markers increased in the second half of gestation. These values reflect an increase in absorption and bone demineralisation [3–5, 19, 20].

In one study, two groups of women underwent bone biopsy during the first trimester of pregnancy and at term. The researchers found bone loss, as evidenced by trabecular thinning at the beginning of the pregnancy, although this bone loss was replaced with new trabeculae at the end of gestation [2].

Some studies have utilised SPA or DEXA during pregnancy. However, there was no evidence of bone demineralisation in these studies. In addition, the studies demonstrated that bone density in nulliparous women in the post-menopausal period was the same as that of pluriparous women and that there was no relationship between pregnancy and increased risk of osteoporotic fractures [21, 22].

Still other studies found temporary bone demineralisation (from 3 to 5%), specifically of the axial skeleton (lumbar vertebrae), the femur, the distal part of the radius, and the hip [22]. In addition, even if there is a small reduction in bone density during pregnancy, there is no clear evidence that this results in long-term effects on the skeleton or subsequent increases in the risk of osteoporotic fractures in postmenopausal women.

The risk of vertebral and femoral fractures is increased in nulliparous women, although the risk of hip fracture decreases by 9% with each pregnancy. This is due to the widening of the external diameter of the proximal femur and of the cortical bone [23–25].

Single-photon absorptiometry or DEXA are inadvisable in pregnancy due to the teratogenic effects on the foetus [1–4, 6].

Quantitative ultrasonometry of the bone, is an inexpensive, radiation-free method that yields information on bone mineral density and quality [26–28]. It is a novel method that allows us to study bone density during pregnancy due to its lack of radiation and thus lack of potential for teratogenic effects on the foetus. Moreover, this technology gives us information about the bone in real time [2].

In our study, we examined phalanges in the distal metaphysis, as this is an area of the body where it is possible to find both trabecular and cortical bone that demonstrates alterations in bone turnover as a result of changes in metabolism [11].

BTT (bone transmission time) is defined as the transmission time between the sent out and received signal. We consider it because it is steady over time and is not impacted by the changes in soft tissue seen in pregnancy (i.e., water retention and weight gain).

Amplitude dependent speed of sound is highly effective in delineating normal bone and demineralised bone [29].

Hellmeyer et al. evaluated a group of 60 women with QUS and found an important progressive reduction of AD-SoS and BTT from the first to the third trimester of pregnancy. They also found a decrease in *z*-score and *t*-score. They were not able to find a relationship between risk factors for osteoporosis or weight gain on QUS parameters [2].

These results agree with those obtained by Aguado et al. in a study on 40 women with QUS that explored daily consumption of dietary calcium. In this study, the decrease of AD-SoS was larger in pregnant women with inadequate calcium intake [30].

In our study of 59 pregnant women, we found a steady decrease in BTT from the first to the third trimester, while we found that AD-SoS decreases between the first and second trimester and then decreases more rapidly at term. We also found that *z*-score and *t*-score decrease more during second and third trimester. We were unable to find a relationship between possible risk factors for osteoporosis (i.e., an increase in BMI, consumption of vitamins, number of previous pregnancies, lactation in previous pregnancies, poor physical activity) and QUS parameters.

We divided the sample into nulliparous and multiparous women and found that AD-SoS is lower at the beginning of the pregnancy in the multiparous group, then increases between the first and second trimester, then decreases during the second and the third trimester (similar to that of the group of nulliparous women).

BTT showed little variation in the group of multiparous women between the first and second trimester; at term, the BTT value is larger than in the group of nulliparous women.

The *z*-score and *t*-score increased during the first and second trimester in the multiparous group and then decreased; a similar pattern was seen in the group of nulliparous women in the third trimester.

UBPI increased during the first and second trimester and then decreased during the second and third trimester. The value of the UBPI is higher in the third trimester than in the first, demonstrating that there is not an increased risk of fracture. In our study, we found that QUS parameters have a different course depending on women who were nulliparous or multiparous.

These results show an important reduction in all ultrasonometry variables with a subsequent increase of remodeling with bone demineralisation in the third trimester of pregnancy. We were unable to find a significant relationship between possible risk factors (i.e., increase of BMI, vitamin intake, number of previous pregnancies, lactation in previous pregnancies, and lack of physical activity) and reduction in QUS parameters. These results show that bone metabolism changes during pregnancy and that this change is different in pluriparous and nulliparous women.

Ultrasonometry is valid, inexpensive, and convenient, which enables the assessment of risk for osteoporosis and, in rare cases, the diagnosis of osteoporosis in pregnancy. In addition, it is radiation-free, thus avoiding the risk of teratogenic effects on the foetus [2, 31–33].

The main limitation of this study is the small sample size, making it difficult to generalise our results on a larger scale to bone metabolism changes in pregnancy. In addition, the accuracy of ultrasonometry is lower than that of DEXA [34].

In future research, we will enlarge our sample size in order to evaluate the maternal skeleton and changes in bone turnover during pregnancy. We aim to determine whether bone turnover varies in multiparous women. In addition, we propose to study women 6 months post-delivery, considering lactation, in order to determine if demineralisation is influenced by breast-feeding.

Conflict of interest statement The authors declare that they have no conflict of interest.

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