Maternal ultrasound bone density in normal pregnancy

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Summary: Objectives: The aim of the study was to investigate the effect of pregnancy on maternal bone mineral density by an ultrasound device.

Study methods: Two hundred and thirty consecutive healthy pregnant women were evaluated by ultrasound densitometry during the 1st (n=45), the 2nd (n=56) and the 3rd (n=129) trimester of pregnancy, measuring the velocity (SoS) and frequency attenuation (BUA) of an ultrasound wave as it passes through the os calcis. Speed of sound (SoS) and Broadmand Ultrasound Attenuation (BUA) values are combined in order to express a relational variable (Stiffness), indicator of bone quality.

Results: Statistically significant reductions in SoS, BUD and Stiffness values were observed during the 3rd trimester vs the 1st and the 2nd trimesters. Negative statistically significant relations were found between the gestational age and ultrasound densitometry parameters.

Conclusion: A linear reduction of ultrasound bone density was observed throughout pregnancy, reaching a statistical significance in the 3rd trimester, when the greatest calcium transfer from the mother to the fetus occurs.

Key words: Ultrasound; Bone density; Bone loss; Pregnancy.

INTRODUCTION

Calcium metabolism in pregnancy is affected by many homeostatic adjustments such as extracellular fluid volume expansion, renal function increase and calcium transport to the fetus ([1, 2]).

The total calcium content of a full-term infant is approximately 32 grams ([3]): the fetal content is related in a linear manner to fetal weight, as shown in Figure 1. At 12 weeks of gestation the fetus weighs approximately 100 grams and has a calcium content of 200 mg: the daily fetal calcium demand rises progressively from 2-3 mg during the 1st trimester to 250 mg and over after the 35th-36th week ([4, 5]).

The potential maternal mineral sources are twofold ([6–8]):

a) the intestinal absorption increase of dietary calcium observed by 20 weeks which is stimulated by higher levels of 1.25 $(OH)_2$-vitamin D_3;

b) the increase of bone turnover (both resorption and formation) mainly as a

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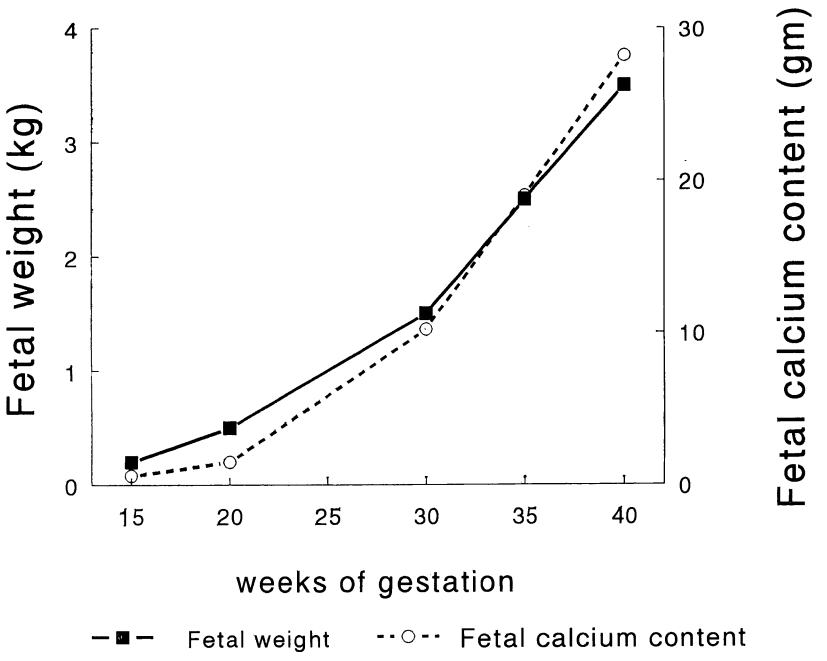

Fig. 1. — Fetal calcium content and fetal body weight in the course of gestation.

consequence of raised levels of PTH, calcitonin and 1.25 $(OH)_2$-vitamin D_3 throughout pregnancy.

Few data are available concerning the effects of pregnancy calcium homeostasis modifications on maternal bone mineral density.

The amount of calcium accumulation during pregnancy only amounts to 2.5% of total maternal body content. Thus any method of measuring maternal bone status needs to be precise enough to reveal more than small differences.

The recently developed Dual Energy Xrays absorptiometry (DEXA) instruments show a very high precision (CV$\approx$2%); however, the use of ionizing radiations, even at very low energy levels, does not allow their application in pregnancy. Nowadays, we can overcome the problem by Ultrasound bone densitometry which is fully radiation-free and shows a very good precision both in vitro and in vivo ([9-10]).

The system (Lunar Achilles) measures, by a computer analysis, the velocity (Speed of Sound, SoS) and frequency attenuation (Broadband Ultrasound Attenuation, BUA) of a ultrasound wave as it travels through the os calcis. Both SoS and BUA correlate highly with BMD in vitro and in vivo ([11-13]).

Furthermore, the Achilles device combines SoS and BUA in a third variable called as "Stiffness" (it is very important to note that this term as utilized here has no relation to the true biomechanical term). With respect to SoS and BUA, Stiffness provides a better diagnostic sensitivity (comparable or superior to DEXA BMD) ([14, 15]), and it correlates more accurately with BMD values ([16]). In our hands, the Achilles densitometer showed a $\leq$ 1.1% CV in vitro and a $\leq$ 1.79% CV in vivo ([17]).

In this paper we present comparative data on the quantitative behavior of ultra-

sound bone densitometry performed in healthy patients at the 1st, the 2nd and the 3rd trimester of pregnancy.

PATIENTS AND METHODS

In this study two hundred and thirty healthy white women were consecutively evaluated during the 1st (n=45), the 2nd (n=56) or the 3rd trimester (n=129) of a singleton physiologic pregnancy whose gestational age had been verified by ultrasound.

No patient had previous evidence of osteoporosis, other metabolic disease, hyper- or hypothyroidism or other problems which could interfere with the interpretation of the data.

Each patient underwent an os calcis densitometry by a Lunar Achilles (Madison, Wisconsin) ultrasound bone densitometer according to the following standard procedure.

The non dominant heel is placed on a shim a chamber with a lid acting as a calf support; the foot is correctly positioned in the center of the chamber with the aid of a toe peg on the shim so the peg is between the patient's big toe and second toe.

Both sides of the heel are previously scrubbed vigorously for 5 seconds each side in order to remove any interfering skin debris. Then a 37° C preheated water soluton cointaining surfactant and antimicrobials enters the chamber and surrounds the heel.

The ultrasound signal is sent from one transducer through the heel immersed in the waterbath and is received by an opposing fixed transducer. The signal is digitized and stored by circuitry in a control box and, when each determination is completed, the stored data are transmitted to an IBM-compatible computer for analysis by the Lunar Achilles software (version 1.4) in order to calculate:

– the *Speed of Sound (SoS):* this measurement involves the determination of the transit time of an ultrasound wave as it passes through the heel and the width of the heel at that site. Transit time is the amount of time elapsed between the beginning of the transmitted wave pulse and the beginning of the received wave pulse measured by counting the number of ticks of a high-frequency crystal controlled clock. The intertransducer distance is obtained by measuring the transit time in distilled water.

– the *Broadband Ultrasound Attenuation (BUA);* this measurement involves sending a broadband ultrasound pulse through the os calcis and quantifying the bone frequency absorption. Since the transducer generates a wave with a wide frequency spectrum, this allows attenuation measurements over a range of frequencies. The net attenuation at each frequency is obtained by subtracting these values from the spectrum of a weakly attenuating reference medium (water). All the points are then plotted in linear regression to obtain the attenuation slope (dB/MHz) which represents the reported BUA value.

– the *"Stiffness":* this relational variable is the result of the software combination of the SoS and the Bud values. The lowest Bud and SoS values are substracted from the observed values in order to provide a scaling that is proportional to the human range of values according to the following formula: Stiflness = $0.67 \times BUA + 0.28 \times SoS\text{-}420$.

This variable is expressed both as Z-score from the expected value for a 20-40 year old healthy woman *(T-score)* and as Z-score from the expected stiffness value of a reference female group of the same age, weight and race *(Z-score)*.

Statistical analysis

Linear regression analysis was used to plot correlations between ultrasound bone densitometry parameters and gestational age. One way analysis of variance and appropriate post-hoc tests were used to compare SoS, BUA and Stiffness values between the 3 different trimester groups.

Homogeneity between the 3 groups as regrads to some clinical and demographic characteristics was tested by the Kruskall-Wallis test.

RESULTS

– *SoS*

A statistically significant negative relation was found ($r = -0.20$; $p = 0.002$) between SoS values and the weeks of gestation (SoS = 1558.77 m/s −0.549 * weeks of gestation) (Fig. 2).

Analysis of variance showed a significantly different behavior of SoS in the 3 trimesters ($p = 0.007$). SoS values were significantly reduced in the 3rd trimester group (1537.61 ± 30.55 m/s) compared with the 1st (1551.78 ± 32.33 m/s, $p = 0.008$) and the 2nd (1549.43 ± 29.59 m/s, $p = 0.01$) (Fig. 3).

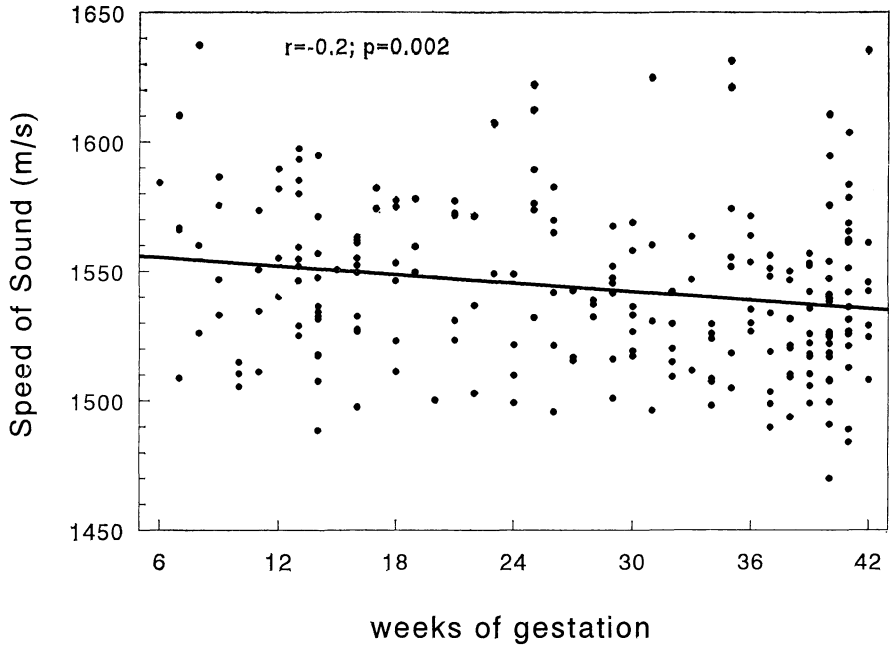

Fig. 2. — Relationship between SoS values and the weeks of gestation.

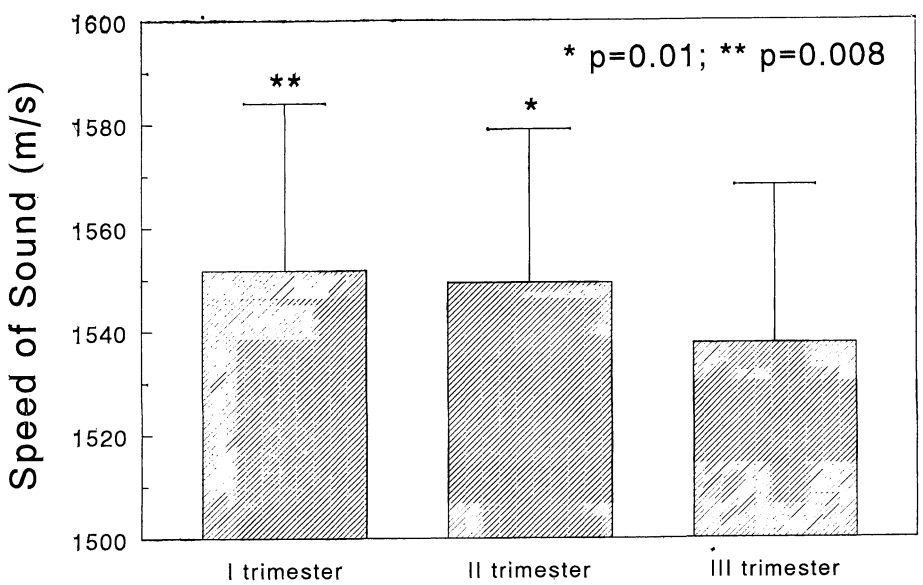

Fig. 3. — SoS quantitative behaviour in the 3 trimesters.

Table 1. – *Demography of the 3 groups.*

GROUP	1st Trimester	2nd Trimester	3rd Trimester	p***
No. of cases	45	56	129	
Age (yrs)	31.2±5.9	29.9±5.3	30.5±5.1	NS
Weight * (kg)	59.7±6.3	58.9±5.9	60.1±6.5	NS
Height (cm)	163.0±6.1	161.5±5.4	163.1±7.0	NS
B.M.I.	22.6±2.3	22.7±2.4	22.7±2.6	NS
Smokers (%)	18.3	16.9	17.5	NS***
Age at menarche (%)	12.0±1.4	12.7±1.6	12.5±1.4	NS
Parity	0.52±0.7	0.59±0.8	0.55±0.8	NS

(*) As recalled before pregnancy (**) Kruskall-Wallis test (***) Chi-square test

– *BUA*

A statistically significant negative relation was found ($r = -0.17$; $p = 0.008$) between BUA values and the weeks of gestation (BUA = 116.89 dB/MHz − 0.159* weeks of gestation) (Fig. 4).

Analysis of variance showed a significantly different behavior of BUA in the 3 trimesters ($p = 0.02$). BUA values were significantly reduced in the 3rd trimester group (110.86±9.34 dB/MHz) compared with the 1st (115.22±10.62 dB/MHz, $p = 0.01$) and the 2nd (113.72 ± 11.39 dB/MHz, $p = 0.05$) (Fig. 5).

– *Stiffness*

– *T-score*

A statistically significant negative relation was found ($r = -0.21$; $p = 0.001$) between this index and the weeks of

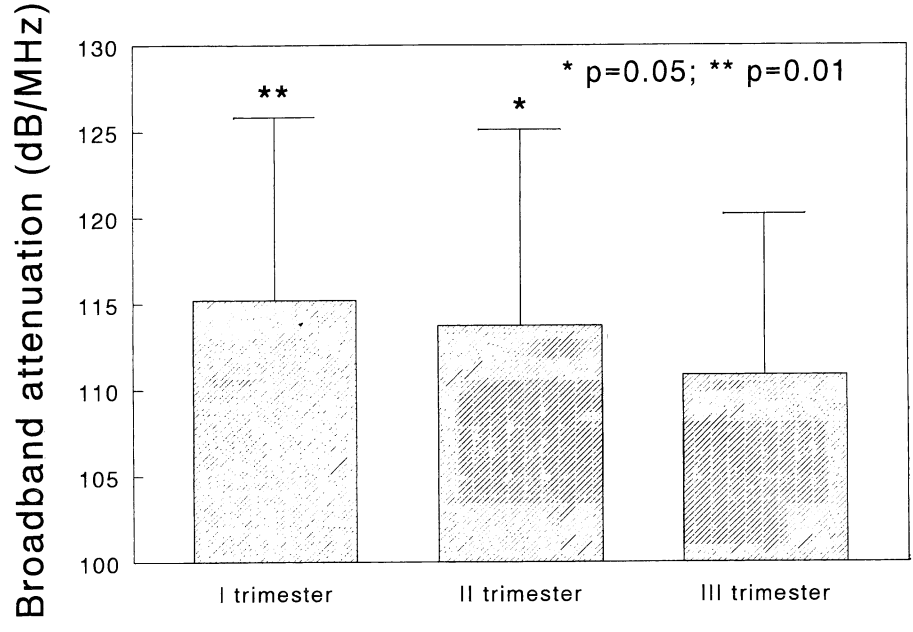

Fig. 4. — Relationship between BUA values and the weeks of gestation.

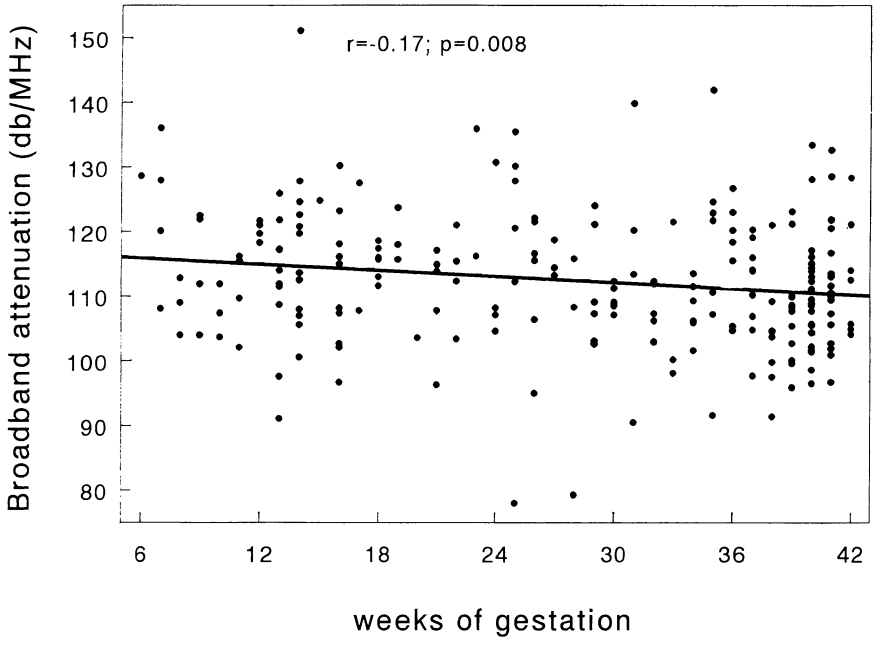

Fig. 5. — BUA quantitative behaviour in the 3 trimesters.

gestation (Stiffness T-score = 0.522 −0.023* weeks of gestation) (Fig. 6).

Analysis of variance showed a significantly different behavior in the 3 trimesters (p=0.003). Stiffness T-scores were significantly reduced in the 3rd trimester group (−1.42±1.25) compared with the 1st (−0.80 ± 1.18, p = 0.003) and the 2nd (−0.95 ± 1.11, p = 0.01) (Fig. 7).

– *Z-score*

A statistically significant negative relation was found (r = −0.24; p = 0.0003) between this index and the weeks of gestation (Stiffness Z-score = −0.094 −0.026 * weeks of gestation) (Fig. 8).

Analysis of variance showed a significantly different behavior in the 3 trimesters (p=0.001). Stiffness Z-scores were significantly reduced in the 3rd trimester group (−0.89 ± 1.26) compared with the 1st (−0.21±1.14, p=0.001) and the 2nd (−0.41±1.12, p=0.01) (Fig. 9).

DISCUSSION

Our data show reduced levels of SoS and BUA throughout pregnancy: both parameters are significantliy related to gestational age in a linear manner; the comparison between groups at 3 different trimesters points out significant reductions in the 3rd trimester versus the 1st and the 2nd trimesters.

Statistical significances increase when we consider Stiffness quantitative behavior, as was reasonable, since it represents a mathematical combination between the two ultrasound measurements. Significance gets the highest when we express this index as Z-score from the expected stiffness value of a reference female group of the same age, weight and race.

We have previously reported that os calcis ultrasound BUA, SoS and "Stiffness" measurements correlate well with trabecular BMD such as lumbar spine or proximal femur density.

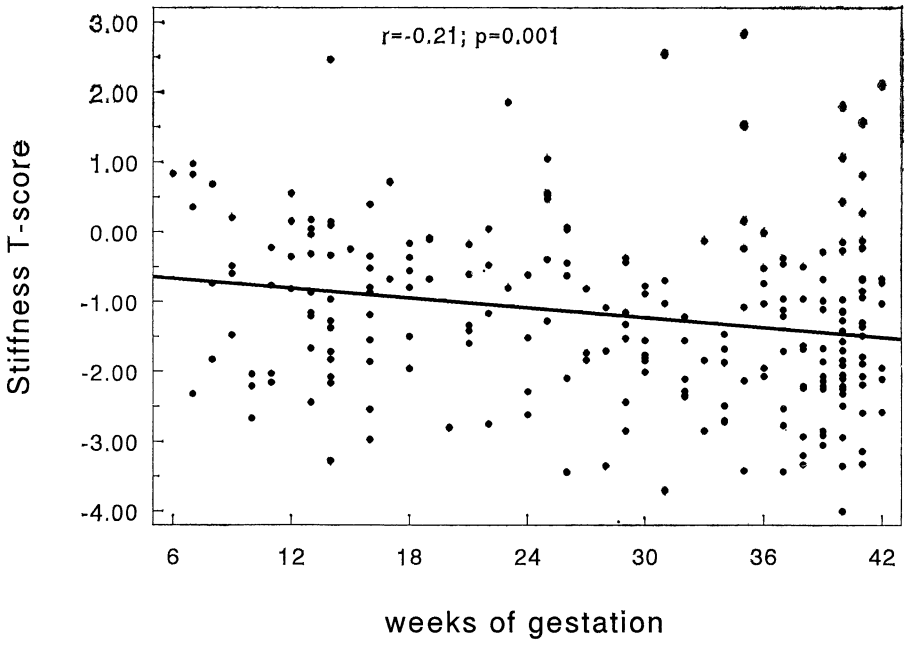

Fig. 6. — Relationship between Stiffness T-scores and the weeks of gestation.

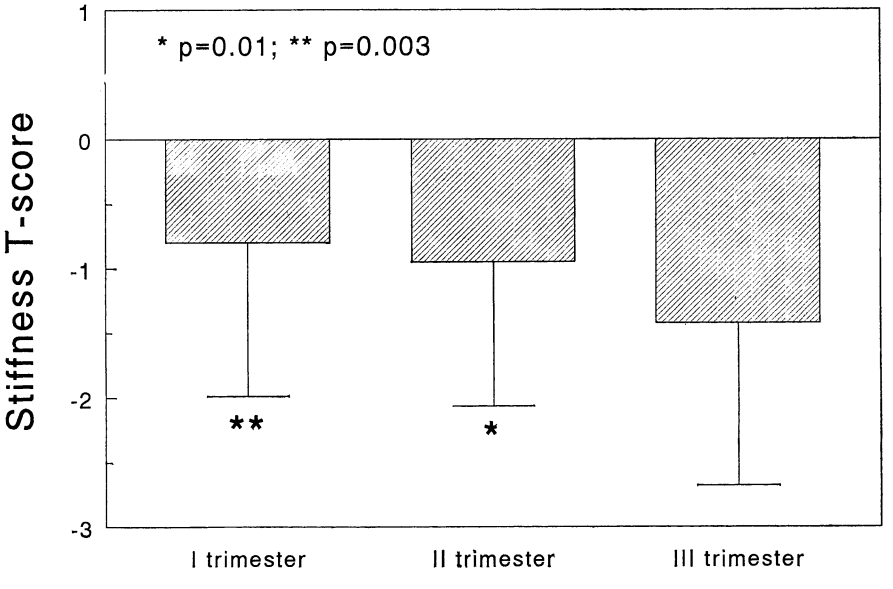

Fig. 7. — Stiffness T-score behaviour in the 3 trimesters.

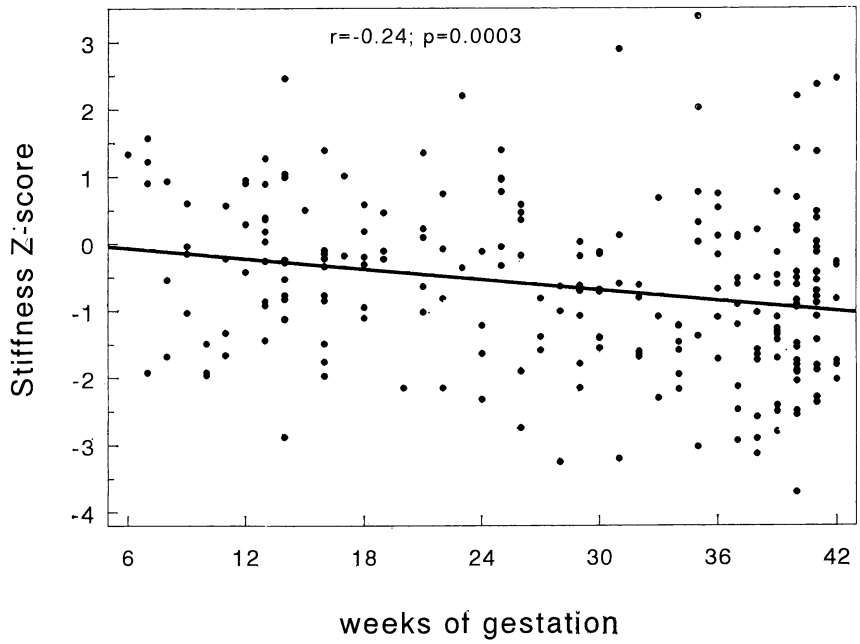

Fig. 8. — Relationship between Stiffness Z-scores and the weeks of gestation.

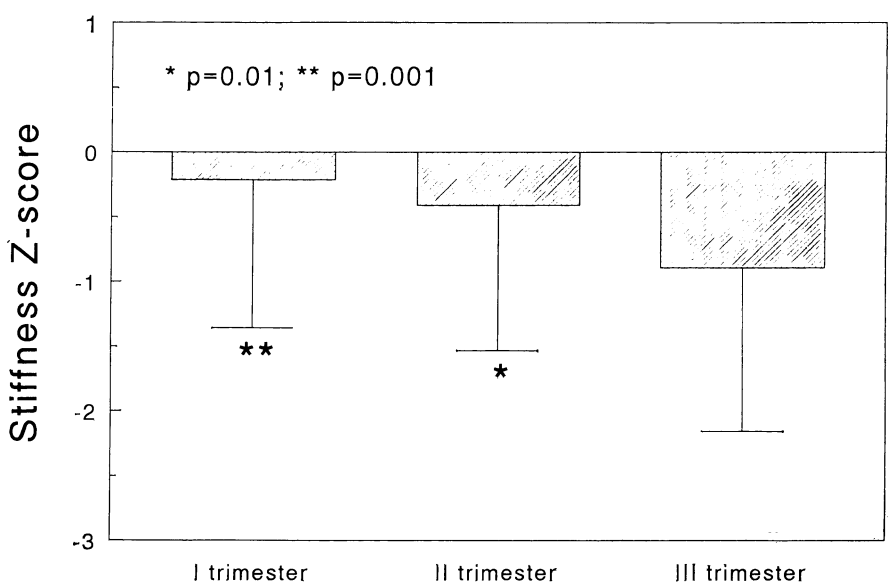

Fig. 9. — Stiffness Z-score behaviour in the 3 trimesters.

Therefore we can at least conclude that a reduction of trabecular bone mass occurs in the course of gestation, thus confirming a previous observation of a 4.2% reduction of ultradistal forearm mineral content made by other Authors ([18]).

However, although bone mass is well known to be highly related to bone strength, its measurement (by electromagnetic ionizing radiations as for DPA, DXA and QCT techniques) is not capable of providing information on the biomechanical competence of the skeleton, which is related to factors other than mass, such as the microstucture and architecture.

As a mechanical traveling vibration, ultrasound can provide several informations on bone structural properties such as its stiffness, brittleness and elasticity. As regards micro-architecture, ultrasound analysis can also give indications as regards to trabecular orientation and histology ([19-21]): velocity is associated with histomorphometric parameters such as bone volume fraction, trabecular number and trabecular separation, while attenuation is significantly related to bone surface/volume ratio and mean trabecular thickness. Low SoS values reflect wide intertrabecular distances with a high number of non connected trabeculae; low BUA values reflect the presence of a high number of short trabeculae.

Going back to our results, it is definitely not easy to understand which factor determines the observed modifications of maternal trabecular bone mass and structure.

If we try by extrapolations to make our ultrasound densitometry data comparable to fetal calcium content values as reported from other Authors ([4, 5]) in the course of gestation, it is easy (and definitely very fascinating) to observe how "stiffness"

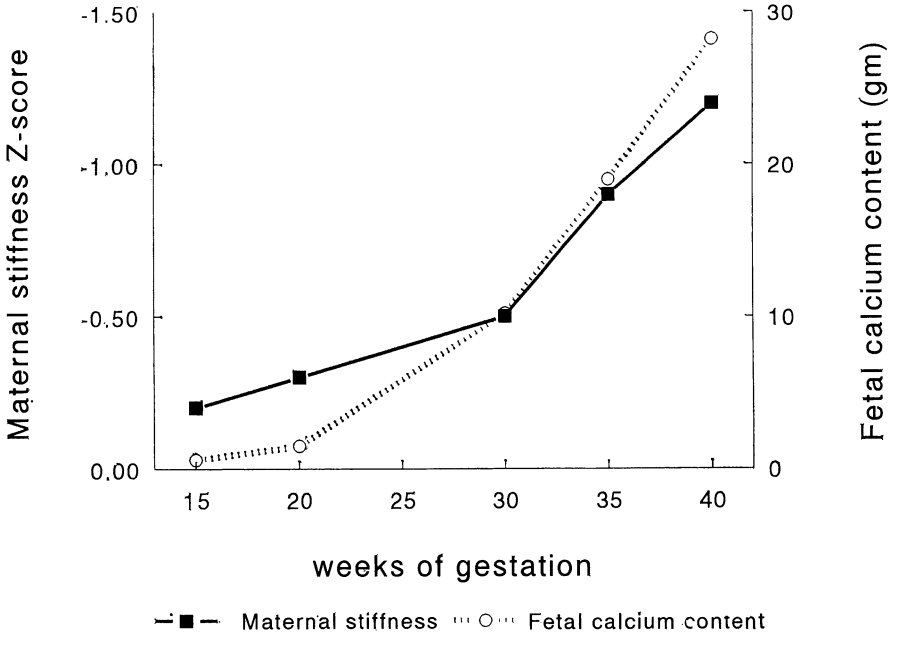

Fig. 10. — Comparison of maternal stiffness Z-score and fetal calcium content behaviour in the course of gestation.

reduction strictly follows fetal calcium store increase (Fig. 10).

As regards calciotropic hormones, the observed increases of circulating level of PTH and 1.25 $(OH)_2$-vitamin D_3 reach their peak during the 3rd trimester of pregnancy ([6, 8]). ^{48}Ca balance and kinetic studies have also shown a remarkable increase of maternal bone resorption between 30 and 40 weeks of gestation ([7]), as confirmed by the observation of higher urinary hydroxyproline excretion levels.

Nor can we avoid hypothesizing further pregnancy hormonal influences on bone remodeling such as those coming from estrogens, hPL or tyroxine ([1]).

Longitudinal studies need to be performed in order to clarify the true amount of maternal bone quality and quantity loss in the course of pregnancy and how much reversible it is after delivery and lactation.

However, the fairly frequent observation of pregnancy induced forms of osteoporosis calls for more attention in order to identify new effective prevention strategies for high risk patients.

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