

Reduction in Bone Loss from 5 to 20 Weeks Postpartum in Adolescents Supplemented with Calcium Plus Vitamin D during Pregnancy Is Not Sustained at 1 Year Postpartum: Follow-up Study of a Randomized Controlled Trial

Maria Eduarda L Diogenes,^{1,2} Flávia F Bezerra,¹ and Carmen M Donangelo³

¹Nutrition Institute, State University of Rio de Janeiro, Rio de Janeiro, Brazil; ²Brazilian National Cancer Institute José Alencar Gomes da Silva, Rio de Janeiro, Brazil; and ³School of Nutrition, University of the Republic, Montevideo, Uruguay

ABSTRACT

Background: Calcium plus vitamin D supplementation of pregnant Brazilian adolescents with habitually low calcium intake (~600 mg/d) reduced bone loss during the first 20 wk postpartum.

Objective: We investigated maternal bone mass changes during the first year postpartum as a follow-up of the clinical trial.

Methods: Pregnant adolescents (14–19 y) received calcium (600 mg/d) plus cholecalciferol (200 IU/d) supplementation ($n = 30$) or placebo ($n = 26$) from 26 wk of gestation until parturition. Bone area and bone mineral content and bone mineral density (BMD) at total body, lumbar spine, and hip (total and femoral neck) were assessed by DXA at 3 time points postpartum (5 wk, 20 wk, and 56 wk). Intervention group, time postpartum, and group \times time interaction effects were tested by repeated-measures mixed-effects models adjusting for calcium intake, return of menses, breastfeeding practices, and body weight.

Results: Time ($P < 0.05$) but not group affected several absolute bone measurements. There was a group \times time interaction for femoral neck BMD ($P = 0.045$). Mean \pm SE values (g/cm^2) at 5 wk, 20 wk, and 56 wk were, respectively, 1.025 ± 0.026 , 0.980 ± 0.026 , and 1.022 ± 0.027 for the placebo group and 1.057 ± 0.025 , 1.030 ± 0.024 , and 1.055 ± 0.025 for the supplemented group. An interaction also was observed for percentage change in femoral neck BMD relative to 5 wk ($P = 0.049$), with a more pronounced decrease in the placebo group ($-4.58 \pm 0.42\%$) than in the supplemented group ($-3.15\% \pm 0.42\%$) at 20 wk ($P = 0.019$), and no difference between groups at 56 wk ($-0.44\% \pm 0.71\%$ in the placebo and $-0.76\% \pm 0.62\%$ in the supplemented group; $P = 0.65$).

Conclusions: Calcium plus vitamin D supplementation of the adolescent mothers reduces the magnitude of bone loss at the femoral neck from 5 to 20 wk postpartum without an effect on bone changes after 1 y postpartum, indicating that there is no sustained effect of the supplement tested. *J Nutr* 2021;151:548–555.

Keywords: bone mineral density, bone health, adolescent mothers, adolescence, lactation, intervention

Introduction

Pregnancy and lactation are periods of increased maternal bone calcium mobilization for fetal growth and breast-milk production, resulting in temporary site-specific bone loss during lactation. In women, this loss is gradually recovered after 6 mo postpartum, irrespective of calcium intake and breastfeeding status (1–4). The skeletal response to pregnancy, lactation, and the postpartum period may be different in adolescent females since bone is actively accruing calcium to reach peak bone

mineral density (BMD) in these very young mothers while simultaneously mobilizing bone calcium for fetal and breast-milk demands (1, 5). In theory, bone status of adolescent mothers is at risk when dietary calcium intake is low and, in this case, it may benefit from calcium supplementation. In practice, only a few long-term postpartum studies addressed these questions in different populations and with different approaches (1, 5–7).

Longitudinal changes in BMD during the postpartum period in adolescent females have been assessed with different study

designs in Brazil (8, 9), Argentina (10, 11), and Mexico (12, 13). Bone loss (1–10%) was observed at 2–6 mo postpartum in most studies, particularly at trabecular bone sites (8–11). These losses were associated with hormonal status (8), frequency of breastfeeding (13), changes in body weight (11, 13), and calcium intake (9, 11). Only a few studies assessed maternal bone status at 12 mo postpartum or later (8, 13, 14).

Bone losses during lactation were almost completely recovered at 12 mo postpartum in adolescent mothers with dietary calcium intake at early lactation ranging from 890–1100 mg/d (12–14), but these were partially recovered at 12–30 mo postpartum in adolescent mothers habitually consuming <500 mg calcium/d (8). Although differences among studies—such as breastfeeding practices, resumption of menses, physical activity, and changes in body weight—may have influenced the postpartum bone responses, taken together, results from these studies suggest that increasing calcium intake could favor long-term bone mass recovery postpartum in adolescents. If this is the case, it remains unclear if calcium intake should be increased during lactation and/or during pregnancy for long-lasting postpartum bone recovery in adolescent mothers. Increased calcium intake after delivery benefitted maternal bone mass indices from 0.5 to 6 mo postpartum of adolescent mothers (11, 15). Similarly, higher dietary calcium intake during the last trimester of pregnancy, when calcium absorption is upregulated, was associated with increased lumbar spine bone z score postpartum in adolescent females (16).

We have previously addressed the effect of calcium plus vitamin D supplementation during pregnancy on bone loss during lactation in a randomized controlled trial conducted in Brazilian adolescent mothers with habitually low calcium intake (9). Results of that study indicated that supplemented mothers had higher lumbar spine bone mass at 20 wk postpartum and reduced rate of bone mass loss at the femoral neck from 5 to 20 wk postpartum than those receiving placebo. We herein report the results of the follow-up of this trial up to 56 wk postpartum in order to investigate the long-lasting effect of calcium plus vitamin D supplementation during pregnancy on maternal bone mass changes during postpartum.

Methods

Subjects and study design

Detailed descriptions of the inclusion and exclusion criteria, study protocol, ethical approval, and results of the clinical trial (NCT01732328) testing the effect of calcium plus vitamin D supplementation during pregnancy on maternal bone mass changes postpartum and on fetal growth and neonate bone mass were previously published (9, 17). Sample size was calculated considering previously reported data of lumbar spine BMD (mean \pm SD: 1.083 ± 0.038 g/cm²) of lactating adolescent mothers (18). It was estimated that a sample size of 25 participants per group is required to detect a difference of 0.03 g/cm² between placebo and supplemented groups, with a significance level of 95% and a statistical power of 80%. The initially randomized sample size was increased accounting for losses due to potential complications

during pregnancy, changes in the intention to breastfeed (a study condition at least in the first postpartum measurement), and the long period of follow-up (~15 mo). The trial was approved by the Ethical Committee of the Maternity School at the Federal University of Rio de Janeiro (Brazil).

Briefly, adolescents who were pregnant for the first time and attending prenatal care (2009–2011) at the Maternity School at the Federal University of Rio de Janeiro were invited to participate in the trial. The pregnant adolescents were randomly assigned by a member of the research team (1:1 ratio within permuted blocks of size 10, participant blinded) to receive a commercially available supplement (Rexall Sundown, Inc., NY) containing calcium (600 mg, as calcium carbonate) plus vitamin D (200 IU, as cholecalciferol) or placebo for daily use from 26 wk of gestation until parturition.

Details on enrollment, losses, and final number analyzed for maternal bone mass measurements at 5 wk, 20 wk, and 56 wk postpartum are shown in Figure 1. Women were excluded if they had chronic health problems (eg, diabetes), were smokers, or users of corticosteroids or nutritional supplements besides iron plus folate supplements provided during standard prenatal care. After randomization, participation was discontinued if there were pregnancy complications or if mothers decided not to breastfeed (Figure 1). Of the 84 adolescent mothers initially assigned to the study, 56 were measured at 5 wk, 47 completed measurements at 20 wk, and 30 completed measurements at 56 wk.

Information on age, prepregnancy BMI, and years elapsed since menarche of the adolescent mothers was obtained at entry in the study (26 wk of pregnancy, baseline). Dietary calcium and vitamin D intakes were assessed by at least three 24-h dietary recall questionnaires during prenatal care visits, and analyzed based on a Brazilian food database (9, 19). At 5 wk, 20 wk, and 56 wk postpartum, maternal body weight, height, and bone mass were assessed, and information on breastfeeding practices and return of menses was obtained.

Anthropometric and bone measurements

Detailed descriptions of the methods used have been published previously (9). Briefly, standing height and body weight were measured by using a stadiometer (Seca) and a calibrated electronic scale (Filizola), respectively. Bone mineral content (BMC), bone area, and BMD of total body, lumbar spine (L1–L4, LS), and hip (total and femoral neck) were assessed using DXA with a Lunar iDXA densitometer and the enCore 2008 version 12.20 software (GE Healthcare). Detailed descriptions of the DXA performance were published previously (9). Bone measurements in total body, lumbar spine, total hip, and femoral neck at 5 wk, 20 wk, and 56 wk postpartum were expressed as absolute values and as percentage change from values at 5 wk postpartum.

Statistical analyses

Comparisons of general characteristics at baseline (26 wk of pregnancy) and at each postpartum time point (5 wk, 20 wk, and 56 wk) between intervention groups (placebo or calcium plus vitamin D) were performed by Student's *t* test for continuous variables and by chi-square test for categorical variables. The effects of intervention group (placebo vs. calcium plus vitamin D), time point (5 wk, 20 wk, and 56 wk postpartum), and intervention group by time point interactions on bone measurements were examined using repeated-measures linear mixed models with Bonferroni post hoc tests. Covariates in the models were defined a priori based on the literature (1, 5) and included calcium intake, return of menses, breastfeeding practices, and body weight. Bone measurement changes from 5 wk to 20 wk and 56 wk were also examined using repeated-measures linear mixed models with the same covariates. Statistical analyses were performed with SPSS 22.0 for Windows software (SPSS, IBM Corp.). Results are reported as means \pm SDs or as means \pm SEs. Values at *P* < 0.05 were considered significant.

Supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq; grant number 471872/2008-3 for CMD and a doctoral fellow to MELD) and Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ; grant number E-26/102.759/2008 to CMD), Brazil.

Author disclosures: The authors report no conflicts of interest.

Data described in the manuscript, code book, and analytic code will be made available upon request, pending application and approval.

Address correspondence to CMD (e-mail: cmarino@nutricion.edu.uy).

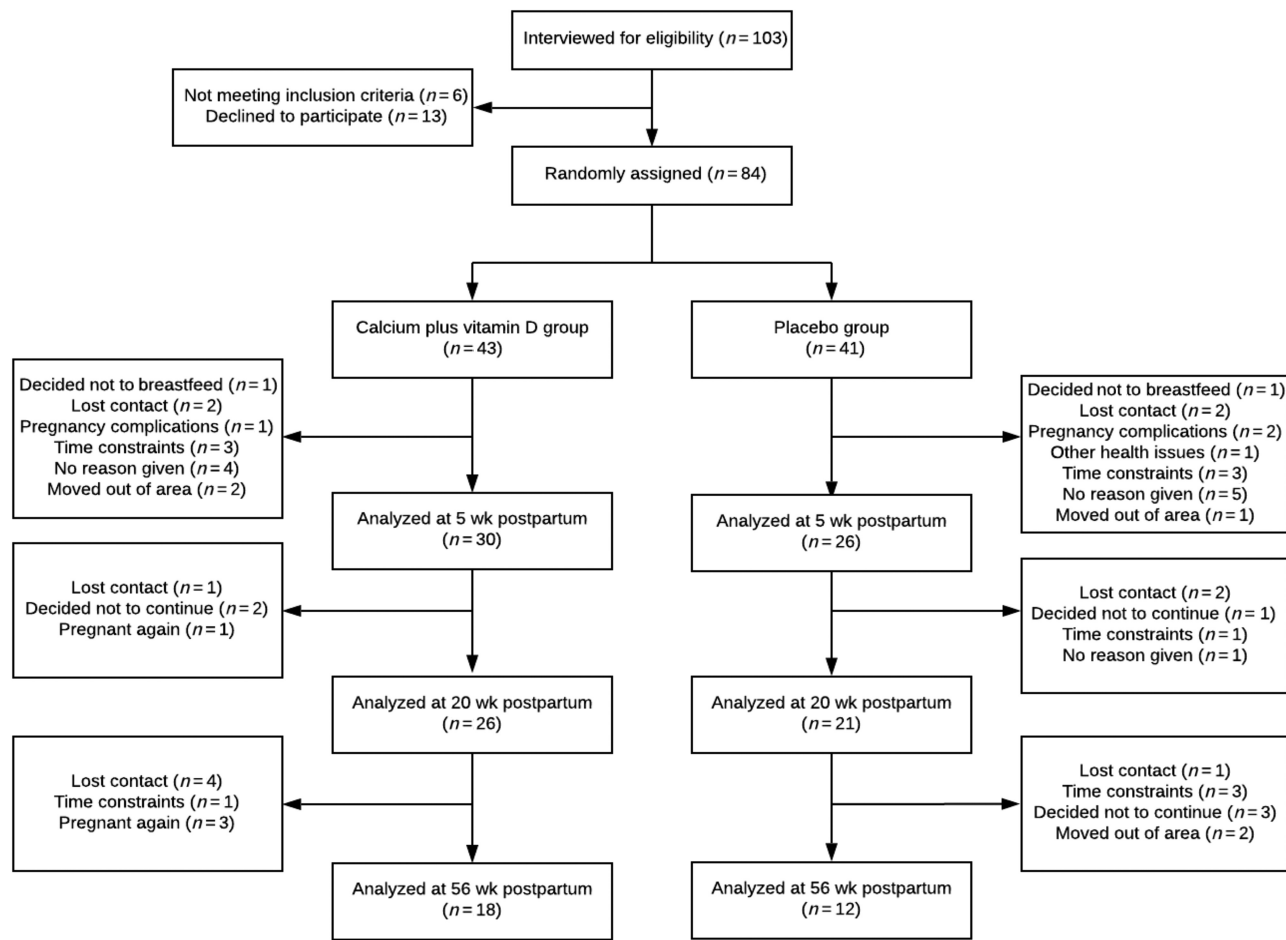


FIGURE 1 Flow diagram of recruitment, random assignment, losses, and follow-up of study participants.

Results

Information on general characteristics at baseline and anthropometry, breastfeeding practices, and return of menses at each postpartum time point are shown according to groups (calcium plus vitamin D and placebo) (Table 1). There were no significant differences in these characteristics between groups except for dietary calcium intake at baseline ($P = 0.02$) and return of menses at 20 wk postpartum ($P = 0.04$). These variables (calcium intake and return of menses) were adjusted for in all subsequent statistical comparisons between groups. Although higher in the placebo group (9), calcium intake was lower than recommended [1300 mg/d (20)] for almost all (93%) the adolescents in this study, with an overall mean calcium intake during late pregnancy of 613 mg/d.

The effects of intervention group, postpartum time point (5 wk, 20 wk, and 56 wk), and group \times time interaction on absolute maternal bone measurements were examined for total body and at specific bone sites adjusted for confounding variables (Table 2). Significant covariates in the models were as follows: body weight (all bone measurements), return of menses (total body bone area), and breastfeeding practice (total body BMC and BMD, lumbar spine BMC and BMD) ($P < 0.05$). Time point was a significant factor on bone measurements ($P < 0.05$), except for bone area at lumbar spine, total hip, and femoral neck ($P > 0.33$). There was a group \times time interaction for BMD at the

femoral neck ($P = 0.045$). Mean differences within each group from 5 wk to 20 wk were -0.044 ± 0.007 g/cm² ($P < 0.001$) in the placebo group and -0.027 ± 0.008 g/cm² ($P < 0.01$) in the calcium plus vitamin D group. Differences from 20 wk to 56 wk were 0.042 ± 0.009 g/cm² ($P < 0.001$) and 0.025 ± 0.007 g/cm² ($P < 0.01$) for placebo and supplemented groups, respectively. The overall calcium plus vitamin D supplement group effect on absolute bone measurements postpartum was not significant (Table 2).

The effects of group, postpartum time point (20 wk and 56 wk), and group \times time interaction on BMD percentage changes from values at 5 wk postpartum were examined adjusted for confounding variables (Figure 2). Significant covariates in the models were as follows: body weight (total hip BMC), return of menses (total body bone area and lumbar spine BMC), and breastfeeding practices (total body BMC and BMD, lumbar spine BMC, bone area and BMD, total hip BMC and BMD) ($P < 0.05$). There was a group \times time interaction for femoral neck BMD percentage changes ($P = 0.049$) (Figure 2D). The percentage decrease from 5 to 20 wk for femoral neck BMD was more pronounced in the placebo group ($-4.58\% \pm 0.42\%$) compared with the calcium plus vitamin D group ($-3.15\% \pm 0.42\%$) ($P = 0.019$). The percentage change from 5 wk to 56 wk did not differ between the placebo ($-0.44\% \pm 0.71\%$) and the calcium plus vitamin D group ($-0.76\% \pm 0.62\%$) groups ($P = 0.65$).

TABLE 1 General characteristics of the adolescent mothers during the study¹

Characteristics	Group		P
	Placebo	Calcium plus vitamin D	
At 26 wk of pregnancy (baseline)			
<i>n</i>	26	30	
Chronologic age, y	17.2 ± 1.0	16.8 ± 1.5	0.31
Time elapsed since menarche, y	5.0 ± 1.7	5.0 ± 2.1	0.91
BMI before pregnancy, kg/m ²	20.9 ± 4.5	21.9 ± 3.4	0.39
Dietary calcium intake, ² mg/d	743 ± 457	500 ± 276	0.02
Dietary vitamin D intake, ² IU/d	32 ± 40	35 ± 38	0.80
At 5 wk postpartum			
<i>n</i>	26	30	
Body weight, kg	59.7 ± 13.3	61.8 ± 11.8	0.54
Height, m	1.61 ± 0.06	1.59 ± 0.06	0.35
Breastfeeding practice, <i>n</i> (%)			0.23
Exclusively	22 (84.6)	23 (76.7)	
Predominantly	4 (15.4)	4 (13.3)	
Complementary	0	3 (10.0)	
At 20 wk postpartum			
<i>n</i>	21	26	
Body weight, kg	56.1 ± 10.3	57.9 ± 9.8	0.54
Height, m	1.60 ± 0.06	1.59 ± 0.07	0.44
Breastfeeding practice, <i>n</i> (%)			0.23
Exclusively	7 (33.3)	3 (11.6)	
Predominantly	9 (42.9)	11 (42.3)	
Complementary	2 (9.5)	6 (23.1)	
No breastfeeding	3 (14.3)	6 (23.1)	
Return of menses (yes), <i>n</i> (%)	8 (38.1)	19 (73.1)	0.04
At 56 wk postpartum			
<i>n</i>	12	18	
Body weight, kg	56.6 ± 12.0	58.7 ± 9.8	0.60
Height, m	1.59 ± 0.06	1.59 ± 0.07	0.85
Breastfeeding practice, <i>n</i> (%)			0.37
Complementary	4 (33.3)	9 (50.0)	
No breastfeeding	8 (66.6)	9 (50.0)	
Return of menses (yes), <i>n</i> (%)	12 (100)	18 (100)	

¹Values are means ± SDs for continuous variables or *n* (%) for categorical variables. Comparisons between groups were determined by using Student's *t* test (continuous variables) or chi-square test (categorical variables).

²Average of three 24-h dietary records obtained between 26 wk of pregnancy and parturition.

Discussion

Recovery of lactation bone loss after 12 mo postpartum has been extensively documented in women (1–4, 21) but few studies have been done in adolescent females (8, 12–14). In contrast to women, the evidence for adolescent females suggests that increasing calcium intake during pregnancy or lactation may contribute to reduce the short-term postpartum bone losses (9, 11, 15, 16). Less is known about the effect of increased calcium intake on long-term postpartum bone changes in adolescent mothers. This is addressed in the present study as a follow-up 1 y postpartum of a randomized controlled trial in Brazilian adolescent mothers with habitual low calcium intake (less than half the calcium DRI) that assessed the effect of calcium plus vitamin D supplementation during pregnancy on bone changes during the postpartum period (9). As described previously, the adolescent mothers who received calcium plus vitamin D supplementation during the last trimester of pregnancy had a reduced magnitude of bone mass loss at the femoral neck from 5 to 20 wk postpartum compared with those receiving placebo. However, there were no significant differences in the overall bone changes after 1 y

postpartum between the placebo and the supplemented groups. This is consistent with no sustained effect over time of the supplementation tested.

Although there were no differences between the placebo and calcium plus vitamin D groups in bone changes from 5 wk to 56 wk, the percentage decrease in BMD at the femoral neck from 5 wk to 20 wk postpartum was more pronounced in the placebo group (–4.58%) than in the calcium plus vitamin D group (–3.15%) (*P* = 0.019). These results indicate that, although calcium plus vitamin D supplementation of the adolescent mothers did not affect the overall bone mass changes from 5 to 56 wk postpartum, it did affect the pattern of transitory bone mass changes during the postpartum period, particularly during the first 20 wk. The physiological maternal bone responses postpartum were attenuated in the group of adolescent mothers who received calcium plus vitamin D supplementation during the last trimester of pregnancy. It is not clear if this reduced maternal bone response postpartum, probably as a result of reduced bone turnover (22), affects other physiological postpartum processes. A reduced bone loss during lactation translates into a transitory better bone density

TABLE 2 Bone measurements of adolescent mothers given placebo or calcium plus vitamin D during the last half of pregnancy at 5, 20, and 56 wk postpartum¹

Variables	Placebo					Calcium plus vitamin D			P value ²		Overall calcium plus vitamin D effect, mean (95% CI)
	5 wk (n = 26)	20 wk (n = 21)	56 wk (n = 12)	5 wk (n = 30)	20 wk (n = 26)	56 wk (n = 18)	Group	Time	Group × time interaction		
Total body											
BMC, g	2089 ± 49 ^a	2056 ± 49 ^b	2083 ± 50 ^a	2129 ± 46 ^a	2103 ± 46 ^b	2138 ± 46 ^a	0.488	<0.001	0.510	48.0 (−89.0, 185)	
Bone area, cm ²	1988 ± 20	1977 ± 19	1989 ± 20	1971 ± 18	1969 ± 18	1981 ± 19	0.677	0.015	0.325	−11.3 (−65.7, 43.0)	
BMD, g/cm ²	1.047 ± 0.019 ^a	1.036 ± 0.019 ^b	1.042 ± 0.020 ^{a,b}	1.076 ± 0.018 ^a	1.065 ± 0.018 ^b	1.076 ± 0.019 ^{a,b}	0.262	<0.001	0.593	−0.031 (−0.024, 0.085)	
Lumbar spine											
BMC, g	50.1 ± 1.76 ^{a,b}	49.5 ± 1.74 ^b	52.5 ± 1.85 ^a	53.6 ± 1.65 ^{a,b}	52.8 ± 1.63 ^b	55.3 ± 1.71 ^a	0.190	<0.001	0.644	3.19 (−1.62, 8.01)	
Bone area, cm ²	46.8 ± 0.88	47.0 ± 0.86	47.9 ± 0.97	48.7 ± 0.83	48.8 ± 0.81	48.8 ± 0.88	0.192	0.579	0.267	1.54 (−0.80, 3.88)	
BMD, g/cm ²	1.067 ± 0.027 ^{a,b}	1.050 ± 0.027 ^b	1.093 ± 0.029 ^a	1.097 ± 0.026 ^{a,b}	1.077 ± 0.025 ^b	1.127 ± 0.026 ^a	0.416	<0.001	0.832	−0.031 (−0.044, 0.106)	
Total hip											
BMC, g	27.7 ± 0.81 ^a	26.8 ± 0.80 ^b	27.6 ± 0.83 ^a	28.2 ± 0.76 ^a	27.7 ± 0.76 ^b	28.5 ± 0.77 ^a	0.505	<0.001	0.257	0.76 (−1.50, 3.01)	
Bone area, cm ²	27.9 ± 0.35	27.8 ± 0.34	27.6 ± 0.37	27.0 ± 0.33	27.0 ± 0.32	27.0 ± 0.34	0.114	0.441	0.176	−0.76 (−1.72, 0.19)	
BMD, g/cm ²	0.990 ± 0.028	0.961 ± 0.028 ^b	1.001 ± 0.029 ^a	1.042 ± 0.026 ^a	1.022 ± 0.026 ^b	1.052 ± 0.027 ^a	0.163	<0.001	0.252	0.055 (−0.023, 0.133)	
Femoral neck											
BMC, g	4.38 ± 0.11 ^a	4.19 ± 0.11 ^b	4.33 ± 0.11 ^a	4.40 ± 0.10 ^a	4.29 ± 0.10 ^b	4.42 ± 0.11 ^a	0.648	<0.001	0.117	0.07 (−0.23, 0.37)	
Bone area, cm ²	4.27 ± 0.06	4.26 ± 0.06	4.24 ± 0.06	4.16 ± 0.06	4.17 ± 0.05	4.20 ± 0.06	0.329	0.992	0.187	−0.08 (−0.24, 0.08)	
BMD, g/cm ²	1.025 ± 0.026 ^a	0.980 ± 0.026 ^{b,3}	1.022 ± 0.027 ^{a,4}	1.057 ± 0.025 ^a	1.030 ± 0.024 ^{b,3}	1.055 ± 0.025 ^{a,4}	0.291	<0.001	0.045	0.039 (−0.034, 0.111)	

¹Values are adjusted means ± SEs unless otherwise indicated. Labeled means (groups combined) in a row without a common letter differ, $P < 0.05$. BMC, bone mineral content; BMD, bone mineral density.

²P values refer to each component of the interaction model (intervention group, time postpartum, and group × time interaction term) in the repeated-measure linear mixed model with calcium intake, return of menses, breastfeeding practices, and body weight as covariates.

³Significant change within group from week 5, $P < 0.01$.

⁴Significant change within group from week 20, $P < 0.01$.

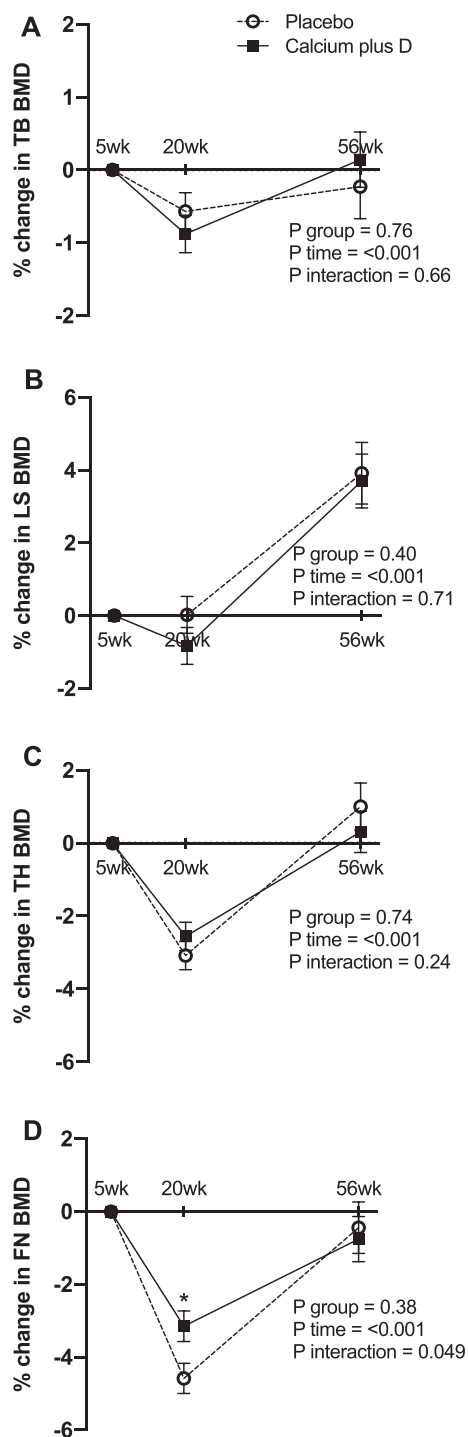


FIGURE 2 (A–D) BMD percentage changes from 5 wk to 20 wk and 56 wk postpartum in the adolescent mothers given placebo or calcium plus vitamin D during the last half of pregnancy. The numbers of subjects at 5, 20, and 56 wk, respectively, were as follows: 26, 21, and 12 in the placebo group and 30, 26, 18 in the supplemented group. All values are adjusted means \pm SEs. *P* values refer to each component of the interaction model (intervention group, time postpartum, and group \times time interaction term) in the repeated-measures linear mixed model, with calcium intake, return of menses, breastfeeding practices, and body weight as covariates. Comparison between groups at each time point was performed for the variable with significant group \times time interaction (FN BMD). *Different from the placebo group, $P = 0.019$. BMD, bone mineral density; FN, femoral neck; LS, lumbar spine; TB, total body; TH, total hip.

status at trabecular sites (9) and might therefore translate into reduced risk of bone fracture in this period. This is particularly important given that bone fractures are highly frequent in adolescents (23). It might also be less detrimental to bone acquisition in the still-growing adolescent mother. On the other hand, a reduced bone loss might result not only in less mobilization of bone calcium but also of other bone mineral components that are essential nutrients during lactation and adolescence, such as zinc (24).

Our study is the first to test the effect of calcium supplementation during pregnancy on maternal bone changes up to 12 mo postpartum in adolescent females. Only 2 previous studies tested this effect in women, in the Gambia (25) and the United States (21), using DXA (25) or peripheral quantitative computed tomography (21) for bone measurements, the latter being not comparable to our bone outcomes. The adolescent mothers in our study had low habitual calcium diet (~ 600 mg/d) and doubled the calcium intake (together with extra vitamin D) during the supplemental period, approaching the recommended 1300 mg/d for adolescents (20). In the Gambian study, habitual dietary calcium was very low (~ 350 mg/d) and the supplemental calcium provided (1500 mg/d) increased over 4-fold their total calcium intake. Bone responses postpartum in our study were notably different from those in the Gambian study. In our study, overall bone changes from 5 wk to 56 wk postpartum did not differ between the calcium plus vitamin D and placebo groups, whereas in the Gambian study, unexpected greater decreases in BMC and BMD at trabecular sites from 2 wk to 52 wk postpartum were observed in the women receiving the calcium supplement compared with placebo. It was suggested that calcium supplementation in pregnant women accustomed to very low calcium intakes may disrupt metabolic adaptation (25) and that the negative effect on the maternal skeleton may persist long term (26). In addition to differences in the amount of calcium in the supplement, complemented or not by vitamin D, other differences including habitual diet, maternal age, and ethnicity might have influenced the divergent responses among studies.

The overall bone recovery during 1 y postpartum observed in our study regardless of intervention was consistent with results from previous studies that found a complete or almost complete bone recovery after 1 y postpartum in adolescent mothers with different habitual calcium intakes (8, 12–14). Taken together, these results suggest that adolescent mothers have physiologic adaptation mechanisms during pregnancy and postpartum that enable them to recover the lactation-associated bone loss irrespective of calcium intake. Other factors such as breastfeeding may be more relevant than calcium intake to bone mass changes postpartum in adolescent mothers. Breastfeeding was a significant covariate for almost all bone outcomes in our study and has been found to be protective of bone health in adolescent mothers in a retrospective nationally representative sample in the United States (27).

The strength of this study was the longitudinal design in an understudied group, adolescent mothers, that allowed us to examine changes in bone mass status during the first year postpartum taking into account well-recognized factors affecting lactation bone loss and postpartum bone recovery, such as breastfeeding practice, return of menses, and postpartum body weight (1, 5, 6).

The study had some limitations. There was a substantial loss of participants over time since randomization (Figure 1). The dropout rate of participants from randomization to the first time point analyzed was 36.6% and 30.2% in the placebo and

supplemented group, respectively. Further losses postpartum were 19.2% and 13.3% from 5 to 20 wk, and substantial losses (42.9% and 30.8%) occurred from 20 to 56 wk in the placebo and supplemented groups, respectively. The motives for these losses are shown in [Figure 1](#). Larger dropouts occurred at longer intervals between measurements. The reason for the uneven loss between groups is unclear since participants remained blinded to treatment at all times. Our results should be interpreted with caution given that the dropout of participants reduced the sample size and limited statistical power to detect differences by group. Evaluating multiple outcomes may have increased the false-positive error rate. Unfortunately, no longitudinal information on dietary intake was available. Nevertheless, studies in Brazilian adolescent mothers indicated that dietary calcium intake is habitually low during lactation (8, 28). We did not ask for specific information on physical activity and chronic alcohol consumption, known to affect bone mass, that may have contributed to residual confounding. However, none of the participants reported alcohol consumption in the three or more 24-h dietary recall questionnaires obtained. Given that there was no nulliparous control group, we cannot conclude that bone mass recovered during the postpartum period in the adolescent mothers studied was similar to those in adolescents who were never pregnant.

In conclusion, this study indicated that supplementation with 600 mg/d calcium and 200 IU/d cholecalciferol during the last trimester of pregnancy in adolescent mothers reduced the magnitude of bone loss from 5 to 20 wk postpartum at the femoral neck, without an effect on overall bone changes after 1 y postpartum. These findings indicate that the benefits of supplementation seen in maternal bone mass during the first 20 wk postpartum (9) are temporary and are not sustained over time. Thus, increasing calcium intake by supplementation during pregnancy to an amount close to recommended (1300 mg/d) may not improve bone recovery during the first year postpartum in Brazilian adolescent mothers with usual low calcium intakes.

Acknowledgments

We thank Dr. Arthur Orlando Correa Schilithz, Brazilian National Cancer Institute José Alencar Gomes da Silva, for statistical advice. The authors' responsibilities were as follows—FFB and CMD: designed the research and had primary responsibility for the final content; MELD: conducted the research; MELD, FFB, and CMD: analyzed the data; CMD, FFB, and MELD: wrote the manuscript; and all authors: read and approved the final manuscript.

References

- Olausson H, Goldberg GR, Laskey MA, Schoenmakers I, Jarjou LMA, Prentice A. Calcium economy in human pregnancy and lactation. *Nutr Res Rev* 2012;25:40–67.
- Sawo Y, Jarjou LM, Goldberg GR, Laskey MA, Prentice A. Bone mineral changes after lactation in Gambian women accustomed to a low calcium intake. *Eur J Clin Nutr* 2013;67(11):1142–6.
- Cooke-Hubley S, Kirby BJ, Valcour JE, Mugford G, Adachi JD, Kovacs CS. Spine bone mineral density increases after 6 months of exclusive lactation, even in women who keep breastfeeding. *Arch Osteoporos* 2017;12:73.
- Kovacs CS. The skeleton is a storehouse of mineral that is plundered during lactation and (fully?) replenished afterwards. *J Bone Miner Res* 2017;32:676–80.
- Bezerra FF, Donangelo C. Calcium supplementation during pregnancy and lactation: implications for maternal and infant bone health.

In: Victor R, editor. Calcium: chemistry, analysis, function and effects. Piccadilly (UK): Royal Society of Chemistry; 2015. pp. 484–508.

- Kovacs CS. Maternal mineral and bone metabolism during pregnancy, lactation, and post-weaning recovery. *Physiol Rev* 2016;96(2): 449–547.
- Grizzo FMF, Alarcão ACJ, Dell'Agnolo CM, Pedrosa RB, Santos TS, Vissoci JRN, Pinheiro MM, Carvalho MDB, Pelloso SM. How does women's bone health recover after lactation? A systematic review and meta-analysis. *Osteoporos Int* 2020;31:413–27.
- Bezerra FF, Mendonça LMC, Lobato EC, O'Brien KO, Donangelo CM. Bone mass is recovered from lactation to post weaning in adolescent mother with low calcium intakes. *Am J Clin Nutr* 2004;80: 1322–6.
- Diogenes MEL, Bezerra FF, Rezende EP, Taveira MF, Pinhal I, Donangelo CM. The effect of calcium plus vitamin D supplementation during pregnancy in Brazilian adolescent mothers: a randomized placebo-controlled trial. *Am J Clin Nutr* 2013;98:82–91.
- Malpeli A, Mansur JL, de Santiago S, Villalobos R, Armanini A, Apezteguia M, González HF. Changes in bone mineral density of adolescent mothers during the 12-month postpartum period. *Public Health Nutr* 2010;13:1522–7.
- Malpeli A, Apezteguia M, Mansur JL, Armanini A, Macías Couret M, Villalobos R, Kuzminczuk M, Gonzalez HF. Calcium supplementation, bone mineral density and bone mineral content: predictors of bone mass changes in adolescent mothers during the 6-month postpartum period. *Arch Latinoam Nutr* 2012;62(1):30–6.
- Sámano R, Morales RM, Flores-García A, Lira J, Isoard F, de Santiago S, Casanueva E. Las adolescentes no pierden densidad mineral ósea en el pós-parto: estudio comparativo con adultas. *Salud Publica Mex* 2011;53:2.
- Mendez RO, Gallegos AN, Cabrera RM, Quihui L, Zozaya R, Morales GG, Valencia ME, Méndez M. Bone mineral density changes in lactating adolescent mothers during the first postpartum year. *Am J Hum Biol* 2013;25(2):222–4.
- Malpeli A, Mansur JL, De Santiago S, Villalobos R, Armanini A, Apezteguia M, González HF. Changes in bone mineral density of adolescent mothers during 12-month postpartum period. *Public Health Nutr* 2010;13:1522–7.
- Chan GM, McMurry M, Westover K, Engelbert-Fenton K, Thomas MR. Effects of increased dietary calcium intake upon the calcium and bone mineral status of lactating adolescent and adult women. *Am J Clin Nutr* 1987;46:319–23.
- O'Brien KO, Nathanson MS, Mancini J, Witter FR. Calcium absorption is significantly higher in adolescents during pregnancy than in the early postpartum period. *Am J Clin Nutr* 2003;78:1188–93.
- Diogenes MEL, Bezerra FF, Rezende EP, Donangelo CM. Calcium plus vitamin D supplementation during the third trimester of pregnancy in adolescents accustomed to low calcium diets does not affect infant bone mass at early lactation in a randomized controlled trial. *J Nutr* 2015;145(7):1515–23.
- Bezerra FF, Cabello GK, Mendonça L, Donangelo CM. Bone mass and breast milk calcium concentration are associated with vitamin d receptor gene polymorphisms in adolescent mothers. *J Nutr* 2008;138:277–81.
- Núcleo de Estudos e Pesquisas em Alimentação (NEPA-UNICAMP). Tabela brasileira de composição de alimentos. Campinas(Brazil): NEPA/UNICAMP; 2006.
- Institute of Medicine. Dietary Reference Intakes for calcium and vitamin D. Washington (DC): National Academies Press; 2011.
- Cullers A, King JC, Loan MV, Gildengorin G, Fung EB. Effect of prenatal calcium supplementation on bone during pregnancy and 1 y postpartum. *Am J Clin Nutr* 2019;109:197–206.
- Ettinger AS, Lamadrid-Figueroa H, Mercado-García A, Kordas K, Wood RJ, Peterson KE, Hu H, Hernández-Avila M, Téllez-Rojo MM. Effect of calcium supplementation on bone resorption in pregnancy and the early postpartum: a randomized controlled trial in Mexican women. *Nutr J* 2014;13(1):116.
- Bishop M, Arundel P, Clark E, Dimitri P, Farr J, Jones G, Makitie O, Munns CF, Shaw N. Fracture prediction and the definition of osteoporosis in children and adolescents: the ISCD 2013 Pediatric Official Positions. *J Clin Densitom* 2014;17(2): 275–80.

24. Donangelo CM, King JC. Maternal zinc intakes and homeostatic adjustments during pregnancy and lactation. *Nutrients* 2012;4(7):782–98.
25. Jarjou LMA, Laskey MA, Sawo Y, Goldberg GR, Cole TJ, Prentice A. Effect of calcium supplementation in pregnancy on maternal bone outcomes in women with a low calcium intake. *Am J Clin Nutr* 2010;92:450–7.
26. Jarjou LMA, Sawo Y, Goldberg GR, Laskey MA, Cole TJ, Prentice A. Unexpected long-term effects of calcium supplementation in pregnancy on maternal bone outcomes in women with a low calcium intake: a follow-up study. *Am J Clin Nutr* 2013;98:723–30.
27. Chantry CJ, Auinger P, Byrd RS. Lactation among adolescent mothers and subsequent bone mineral density. *Arch Pediatr Adolesc Med* 2004;158:650–6.
28. Bezerra FF, Laboissiere FP, King JC, Donangelo CM. Pregnancy and lactation affect markers of calcium and bone metabolism differently in adolescent and adult women with low calcium intakes. *J Nutr* 2002;132:2183–7.