Adiposity and other factors predicting recovery of bone density at 12 months post GDM pregnancy

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Introduction

- Gestational diabetes mellitus (GDM) and type 2 diabetes mellitus (T2DM) share several risk factors[1]. Both are characterized by relative insulin deficiency and insulin resistance[2], and associated with adverse impacts on bone health.[2]
- In pregnancy, maternal bone is resorbed to supply fetal calcium demands for skeletal development.[3] This resorption persists into the postpartum lactation period.[3]
- Postpartum recovery of bone mineral density (BMD) occurs more rapidly with shorter durations of breastfeeding, higher maternal BMI, and adequate vitamin D levels.[4]
- In T2DM, individuals tend to have elevated BMD yet poor bone microstructure and composition ultimately resulting in increased fracture risk[6]. This is influenced by the duration and severity of T2DM.[5]
- TBS is a novel marker of bone health, derived from DXA images of the lumbar spine. It provides an indirect measure of bone microarchitecture.[6]

Aims

- Identify whether a postpartum GDM cohort has lower BMD compared to the age and weight-matched general population at 12 months postpartum
- Determine factors influencing BMD at 12 months postpartum, and factors influencing the recovery of BMD between 3 and 12 months.
- Identify factors which influence the trabecular bone score (TBS) at 12 months, and recovery of TBS between 3 and 12 months

Methodology

- Participants were recruited from the GDM Antenatal Clinic at Blacktown and Mt. Druitt Hospital between 2012 - 2017.
- Inclusion criteria: 1) women>18 years with GDM during recent pregnancy, 2) able to complete an oral glucose tolerance test (OGTT) at the study centre in the postpartum period, 3) able to understand the procedures and requirements of the study and provide informed consent.
- Demographic and lifestyle questionnaires, anthropometric measurements, OGTT, blood tests, and DXA scans were performed at 10 to 12 weeks, and 12 months postpartum
- Analysis: Results are reported as mean ± standard error of the mean (S.E.M) unless specified otherwise. Linear correlations were used to determine the linear relationship between continuous variables. Student t-test was used to determine significance for categorical variables with two factors. ANOVA was used to test significance for categorical variables with more than two factors. Simple regression was used to identify continuous variables which significantly influenced bone health. Multiple regression was then used to determine which of these influential variables were independent predictors of bone health.
- P values <0.05 were considered statistically significant.

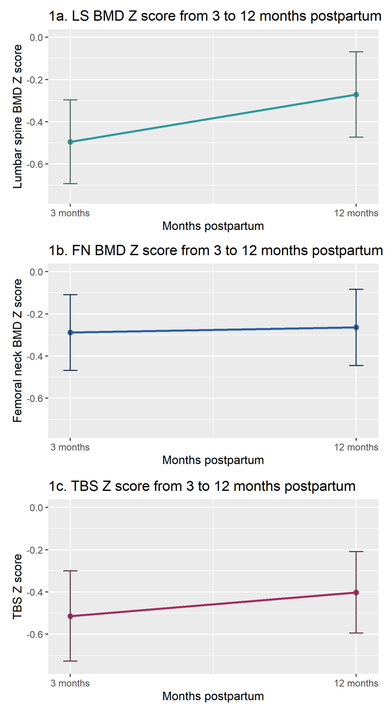
Results

- 101 women completed anthropometric measurements, OGTT, DXA scan, and lifestyle questionnaires at an average of 58.2 ± 9.1 weeks postpartum. The cohort characteristics are summarized in Table 1.
- At 3 months postpartum, mean BMD Z-scores for the lumbar spine (LS) (-0.49 ± 1.00 [SD]), femoral neck (FN) (-0.29 ± 0.91), and TBS (-0.51 ± 1.08) were below the expected mean of 0. At 12 months postpartum, BMD and TBS Z scores improved non-significantly and remained under 0 with LS measuring -0.27 ± 1.02, FN -0.26 ± 0.92, and TBS -0.40 ± 0.97. (Figure 1.)
- Cross-sectional analysis at 12 months postpartum found negative correlations between total body fat % and: LS Z score (r=-0.31, p=0.001), and FN Z score (r=-0.23, p=0.02), and between central fat % and LS Z score (r=-0.28, p=0.005), and FN Z score (r=-0.21, p=0.04) (Figure 2.)
- Longitudinal analysis identified significant negative correlations between change in total body fat % and change in LS Z score (r=-0.275, p=0.006), and change in total body fat % and change in FN Z score (r=-0.412, p<0.001) (Figure 3.)

Table 1. Summary of cohort characteristics at 12 months postpartum

Data	Mean ± SD or Number (%)
Age (years)	34.1 ± 5.1
Ethnicity	
Caucasian	34 (33.7%)
Subcontinental	32 (31.7%)
Asian	19 (18.8%)
Other	16 (15.8%)
Weight (kg)	72.6 ± 15.7
Height (cm)	160.4 ± 6.3
BMI (kg/m²)	28.1 ± 5.3
Lumbar spine BMD (g/cm²)	1.19 ± 0.13
Lumbar spine BMD Z-score	-0.27 ± 1.02 95% Confidence interval (CI): -0.47 to -0.07
Femoral neck BMD (g/cm²)	0.99 ± 0.12
Femoral neck BMD Z-score	-0.26 ± 0.92 95% CI: -0.44 to -0.08
TBS lumbar spine	1.40 ± 0.10
TBS lumbar spine Z-score	-0.40 ± 0.97 95% CI: -0.59 to -0.21

Figure 1. Change in bone health markers from 3 to 12 months postpartum



Results

- Simple regression showed that change in BMI, change in total body fat %, and change in central fat % were all significant negative predictors of change in LS BMD Z scores, and FN BMD Z scores from 3 to 12 months (Table 2.)

Figure 2. Cross-sectional analysis of BMD Z scores and measures of adiposity at 12 months postpartum

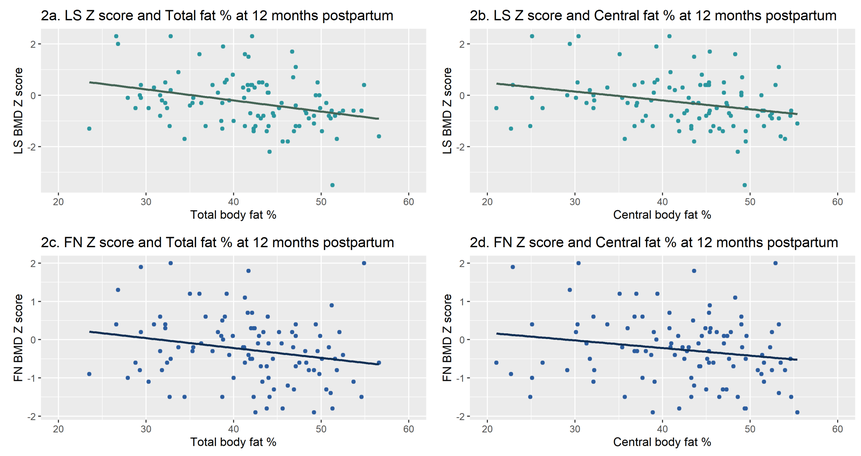


Figure 3. Longitudinal analysis of BMD Z scores, TBS and measures of adiposity from 3 to 12 months postpartum

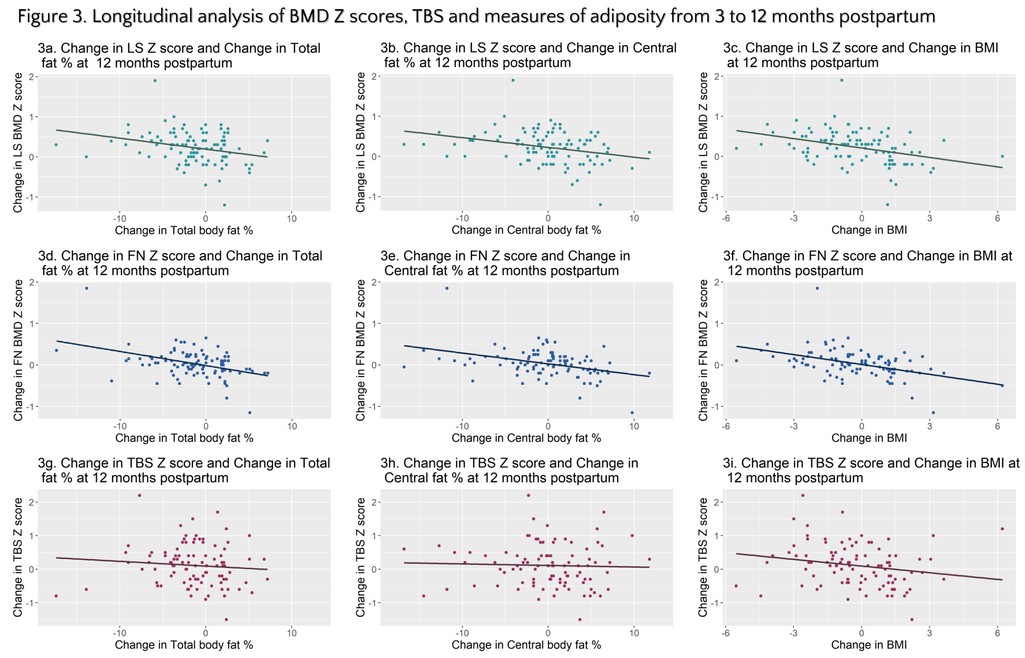


Table 2. Simple linear regression results for LS and FN BMD Z scores, BMI, and measures of adiposity

LS BMD Z-score	Intercept	Beta	Beta 95% CI	P-value	R squared
Change in BMI	0.210	-0.078	-0.119 to -0.038	0.0002	0.132
Change in total body fat %	0.193	-0.027	-0.047 to -0.008	0.0057	0.075
Change in central fat %	0.227	-0.024	-0.040 to -0.009	0.0024	0.090
FN BMD Z-score	**Intercept**	**Beta**	**Beta 95% CI**	**P-value**	**R squared**
Change in BMI	0.012	-0.079	-0.112 to -0.047	0	0.197
Change in total body fat %	-0.014	-0.034	-0.049 to -0.019	0	0.169
Change in central fat %	0.028	-0.026	-0.038 to -0.014	0.0001	0.151

- Women of an Indian ethnicity had greater increases in FN BMD than those from a Caucasian or East/South-east Asian ethnicity from 3 to 12 months postpartum (p=0.009)
- Exclusively breastfeeding at 12 months was linked with greater decreases in FN BMD compared to exclusive formula feeding and mixed feeding (p=0.002)
  - Breastfeeding for ≤6 months was linked with greater increases in FN BMD than breastfeeding for >6 months (p=0.018)
- Insufficient vitamin D levels were associated with greater increases in TBS Z score than sufficient levels (p=0.038)
- There was no relationship between calcium intake, diabetes status, exercise intensity, and LS Z score, FN Z score, and TBS
- On multiple regression, adjusting for calcium intake, breastfeeding status at 12 months, vitamin D level at 12 months and change in HbA1c, **change in BMI remained an independent negative predictor of LS (β= -0.072, p=0.008), and FN (β= -0.068, p=<0.0001) BMD Z scores, and TBS Z scores (β= -0.084, p=0.0113)**

Conclusion

- Greater increases in BMI and adiposity were associated with reduced LS and FN BMD Z scores and less BMD recovery at 12 months after a GDM pregnancy, independent of breastfeeding, and vitamin D status
- Further research investigating the underlying mechanisms for these relationships and identifying key points of intervention are essential for promoting good bone health in women following a GDM pregnancy

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