

Advanced Paternal Age And Offspring Bone Health; An Inverse Relationship

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Introduction

Previous studies highlight that maternal lifestyle and health during pregnancy impact offspring health. For example, advanced maternal age has been associated with greater fracture risk and lower bone mineral density in offspring.^{1,2}

Emerging evidence suggests an impact of paternal factors on offspring later life musculoskeletal health; however, few human studies have been conducted.^{3,4,5} Therefore, this study aimed to investigate associations between paternal age at childbirth and offspring bone health.

Methods

Study design: The Vitamin D in Pregnancy Study a mother-child pair prospective cohort study⁶

Inclusion criteria:

- Paternal date of birth provided at the recruitment visit (<16 weeks gestation)
- Offspring Dual X-ray Absorptiometry (DXA) measurements at 11-year follow up visit

Total number of included pairs: 89

Primary outcomes:

- Total body less head (TBLH) bone mineral density (BMD)
- Total body less head bone mineral content (BMC)
- Spine (L2L4) BMD
- Spine (L2L4) BMC

Analysis: Linear regression models were developed to examine associations. Final models included the outcome of interest, paternal age, and any of the following predictors that were significant in stepwise regression:

- Paternal socioeconomic status (SES)
- Paternal education
- Paternal body mass index (BMI)
- Offspring height at 11 years of age
- Offspring weight at 11 years of age

Ethics:

Barwon Health Human Research Ethics Committee (Project 01/43)



Figure 1: A study participant undergoing a DXA scan at the spine

Results

Demographics

- Of the included 89 pairs, the median age of fathers at childbirth was 32.2 (IQR 29.4-36.7)
- There were 45 (50.6%) male and 44 (49.4%) female offspring
- The median offspring TBLH BMD, TBLH BMC, L2L4 BMD and L2L4 BMC at 11 years of age are 0.84g/cm² (0.78-0.88), 1145.1g (956.9-1372.6), 0.83g/cm² (0.76-0.89) and 25.0g (21.6-29.3), respectively

Table 1: Linear regression analysis of paternal age and offspring bone health measures

	TBLH BMD (g/cm ²)		TBLH BMC (g)		L2L4 BMD (g/cm ²)		L2L4 BMC (g)	
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
Paternal age	-0.002 (-0.004- -0.0005)	0.014	-5.9 (-10.5- -1.3)	0.013	-0.002 (-0.006-0.002)	0.34	-0.17 (-0.3- -0.01)	0.037
Child's weight	0.003 (0.003-0.005)	<0.001	15.2 (11.8-18.6)	<0.001	-	-	0.1 (-0.002-0.2)	0.054
Child's Height	0.003 (0.002-0.005)	<0.001	16.9 (12.4-21.5)	<0.001	0.008 (0.005-0.01)	<0.001	0.5 (0.4-0.7)	<0.001

Linear regression

- Every 5 year increase in paternal age was associated with a mean 1.2%, 2.6% and 3.4% decrease in TBLH BMD, TBLH BMC and L2L4 BMC, respectively (Table 1)
- Paternal SES, BMI, and education were not significant in any models
- There was no association with L2L4 BMD
- A sex interaction term (offspring sex*paternal age at childbirth) was not significant for TBLH BMD, TBLH BMC or L2L4bmc (p=0.22-0.87)
- A sex interaction term was significant with L2L4 BMD (p=0.003). Thus, further analysis was stratified by sex
- Paternal age at childbirth remained not significantly associated with L2L4 BMD in sex stratified models (p=0.12 and 0.26 for females and males, respectively)

Summary:

Every 5-year increase in paternal age was associated with a mean 1.2%, 2.6% and 3.4% decrease in offspring TBLH BMD, TBLH BMC and L2L4 BMC at 11 years of age

Discussion

- To our knowledge, only one other study has investigated associations between paternal age and offspring bone health measures⁷
- Our findings are in the same direction as the above paper; however, they studied associations between paternal age and BMD z scores in children conceived using different assisted reproductive technology methods
- Increasing paternal age has also been associated with increased height of children and increased musculoskeletal abnormalities^{8,9,10}

- As peak bone mass plays a significant role in the risk of developing osteoporosis in later life, these findings are of potential clinical significance¹¹
- A strength of the study is the objective measure of offspring bone health
- A limitation is the small sample size of 89 father-child pairs
- There may be other residual confounding, including further childhood lifestyle measures, that were not included in adjusted analysis

Conclusion

- Advanced paternal age was associated with poorer TBLH BMD, TBLH BMC and L2L4 BMC in the offspring
- Health professionals and prospective parents should consider the father's age as poorer offspring bone health appears to be a consequence of advancing paternal age

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