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Are birth characteristics related to bone quality measures in young adults? The HUNT study, Norway

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Abstract

Summary This population-based study investigated the association between birth characteristics and DXA-derived bone quality in 2,680 young adults (aged 20–54 years). Higher birth weight and length were positively associated with bone strength measures, while associations with buckling ratio and hip axis length were weaker and less consistent.

Purpose To investigate the association between birth characteristics and bone quality indicators from dual-energy X-ray absorptiometry (DXA) in young adults.

Methods This population-based study included 2,680 participants (60% women), aged 20–54 years, from the Trøndelag Health Study (HUNT3 and HUNT4), linked with birth data from the Medical Birth Registry of Norway. Birth characteristics included birth weight, birth length, and birth weight relative to gestational age and sex (categorized as small, appropriate, or large for gestational age). Linear regressions assessed associations with bone quality measures, including cross-sectional area, cross-sectional moment of inertia, buckling ratio, and hip axis length. Analyses were adjusted for sex, birth year, age at DXA scan, gestational length, and adult height (for buckling ratio and hip axis length). Additional analyses included bone mineral density (BMD) to assess direct effects.

Results Higher birth weight and length were positively associated with cross-sectional area and cross-sectional moment of inertia. For each SD increase in birth weight and length, CSA increased by 4.33 and 4.29 mm^2, and CSMI by 0.74 and 0.45 mm^4, respectively. After BMD adjustment, these associations were attenuated for both birth weight (CSA: 1.90 mm^2; CSMI: 0.55 mm^4), and birth length (CSA: 2.13 mm^2; CSMI: 0.58 mm^4). Buckling ratio and hip axis length showed weaker and less consistent associations with birth characteristics, but the association of birth weight and small for gestational age with buckling ratio was somewhat strengthened after adjustment for BMD.

Conclusion Birth characteristics are associated with both bone strength and geometry in young adulthood. These associations are partly independent of BMD, highlighting the value of DXA-derived bone quality measures in assessing skeletal health.

Keywords Birth characteristics · Bone geometry · Bone mineral density · Dual-energy X-ray · Hip structural analysis · Skeletal health

Introduction

Early-life factors, such as birth weight and gestational age, have been associated with bone health and fracture risk later in life [1, 2]. Several studies suggest that birth weight has an impact on long-term skeletal consequences, including reduced bone mass [3, 4].

Bone mineral density (BMD) of the proximal femur, measured by dual-energy X-ray absorptiometry (DXA), is the reference standard for diagnosing osteoporosis [5, 6]. While BMD provides an indirect estimate of bone strength and accounts for approximately 60–70% of its variation [7], this also indicates that other factors contribute significantly to bone strength. Therefore, the definition of osteoporosis also includes bone quality, as BMD alone does not fully reflect the structural integrity of bone [8]. Notably, most fragility fractures occur in individuals without osteoporosis [9, 10].

To better understand fracture risk, it is important to also consider bone quality, such as bone geometry and microarchitectural integrity. These parameters contribute to a more comprehensive assessment of bone strength beyond that

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Extended author information available on the last page of the article captured by BMD [7]. Using hip structural analysis from DXA, geometric indices can be derived to assess biomechanical bone strength [11]. These include, among others, cross-sectional area (CSA), which reflects the bone's resistance to axial compression; cross-sectional moment of inertia (CSMI), which indicates resistance to bending; buckling ratio (BR), an index of structural stability derived from femoral neck width and estimated cortical thickness; and hip axis length (HAL), defined as the distance from the base of the greater trochanter to the inner pelvic rim [12, 13]. CSA and CSMI reflect bone strength and mass distribution, while BR and HAL capture structural vulnerability and geometry.

Previous studies have shown that measures of bone quality predict hip fracture risk independently of BMD [13–15]. These studies found lower CSA and CSMI, along with higher BR and longer HAL, among postmenopausal women who experienced hip fractures. Combining bone quality measures with BMD appeared to improve the accuracy of risk prediction [13–15]. Additionally, a smaller study identified an association between longer HAL and hip fractures in premenopausal women [16].

While the association between birth characteristics and bone mineral density has been studied [3, 4, 17–23], the relationship between birth characteristics and bone quality remains unexplored. To our knowledge, no previous studies have explored the relationship between birth characteristics and DXA-derived bone quality measures in young adults. In older adults, one study of 333 individuals (60–75 years of age) assessed with DXA [24], and another including 650 men (65 years and older) assessed using Quantitative computed tomography (QCT) [25], have found links between early growth and femoral geometry based on self-reported birth weight. The DXA study reported associations between lower birth weight and reduced femoral width, lower CSMI, preserved neck length, and increased buckling ratio, suggesting reduced mechanical strength of the proximal femur, while the QCT study found that lower birth weight was linked to reduced CSA and CSMI and increased femoral neck length.

Our study aimed to provide new insight into early predictors of bone health by combining DXA data from a large population-based cohort with detailed birth information, including birth weight, birth length, and birth weight relative to gestational age and sex. We hypothesized that being born preterm, with low birth weight (LBW) or small for gestational age (SGA) will result in suboptimal bone quality measures.

Material and methods

Study population and data sources

We used participant data from the third and fourth surveys of the population-based Trøndelag Health Study (HUNT) linked with data from the medical birth registry of Norway (MBRN) through the unique national 11-digit personal identification number given to all residents.

Medical birth registry of Norway

Data regarding birth characteristics was obtained from the MBRN. Established in 1967, the MBRN is a mandatory national health registry that gathers details on all births reported by maternity units across Norway, including home births [26]. This registry includes the names and personal identification numbers of both the newborn and the parents, along with information about the mother's health prior to and during pregnancy, as well as mode of delivery and any complications related to birth. Additionally, it records various health metrics in the newborn, including birth length, weight, head circumference at birth, and the Apgar score, among other factors.

The Trøndelag health study

The Trøndelag health study (HUNT) is a longitudinal population-based health study where all inhabitants aged 20 years and older in the region of Nord-Trøndelag, Norway, have been invited to participate in repeated surveys since 1984 [27]. So far, four surveys have been conducted at 11-year intervals. In this study, we used data from HUNT3 (2006–2008) and HUNT4 (2017–2019), with a participation rate of 54% in both surveys [28]. Each HUNT participant underwent a brief clinical examination and completed comprehensive questionnaires. Additionally, based on various selection criteria, subsamples were selected for further examinations, including bone densitometry. In HUNT3, participants were selected to bone densitometry in two different ways: 1) a 10% random sample was drawn among all participants or as part of a 30% random sample from the female birth cohorts, and 2) a symptom sample was selected for the HUNT Lung Study [27], where participants invited to participate in spirometry measurements were also asked to participate in bone densitometry [29]. All bone densitometry examinations in HUNT3 were performed using the GE Lunar Prodigy Advance machine. In HUNT4, individuals who had undergone bone densitometry in HUNT2 and/or HUNT3 and were still living in the region were invited for new examinations. In HUNT4, DXA was measured using both the Lunar Prodigy and Hologic Horizon machines, but to ensure consistency, only data from the Lunar Prodigy was included in the present study.

Our study included a total of 2,680 participants (1,596 women and 1,084 men) born between 1967–1997, with bone densitometry and available birth characteristic information. We included the first available bone measurement for each participant, using data from HUNT

3 ($N=2{,}412$ participants) when available, and from HUNT 4 ($N=435$) otherwise. Measurements from the left hip were used as the reference standard. If left hip data were missing, right hip measurements were included ($N=3$ for CSA, CSMI, and BR; $N=247$ for HAL). The inclusion and exclusion criteria are illustrated in the flowchart (Fig. 1).

Exposure: birth characteristics

Birth weight

Analyzed as a continuous variable (per 100 g or standard deviation) and interval scale. Interval scale: < 2.5 kg (low birth weight, LBW) [30]; 2.5–2.9 kg; 3.0–3.4 kg; 3.5–3.9 kg (reference group, representing the average birth weight in Norway [31]); ≥ 4.0 kg (high birth weight, HBW).

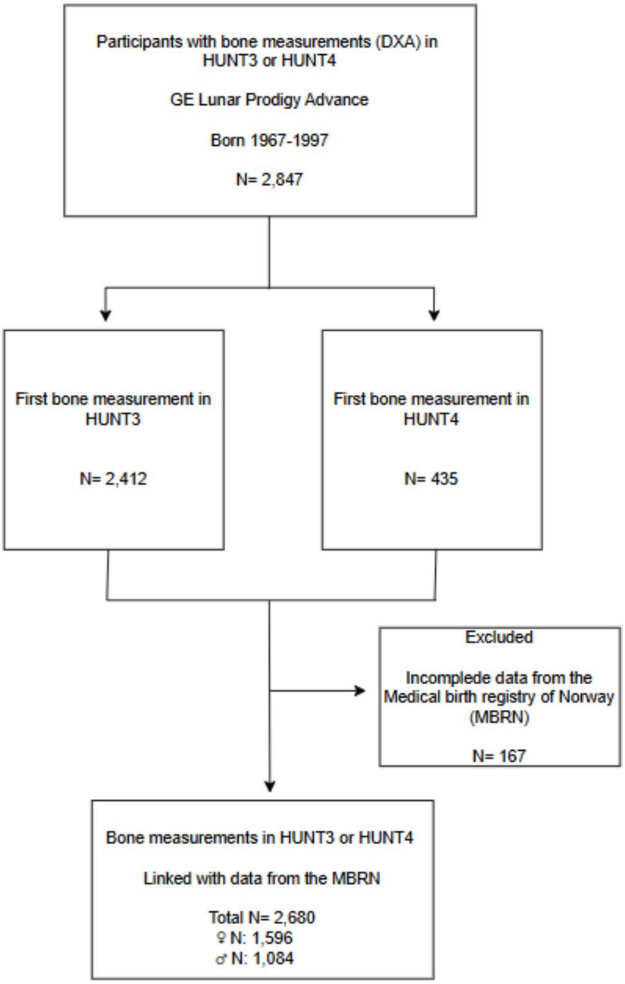

Fig. 1 Flowchart of participants with bone densitometry data from HUNT3 and HUNT4 linked to birth registry information (N = number of participants)

Birth length

Analyzed as a continuous variable (per cm or standard deviation) and interval scale. Interval scale: < 47 cm (low birth length), 47–53 cm (reference group, representing average birth length [31]) and > 53 cm (long birth length).

Birth weight relative to gestational age and sex

Assessed using sex- and gestational age-specific standardized birth weight z-score [32], calculated based on gestational age from the last menstrual period. Categories were defined as follows: small for gestational age (SGA), defined as birth weight below the 10th percentile (z-score less than − 1.28 standard deviations (SD)); appropriate for gestational age (AGA), defined as birth weight between the 10th and 90th percentiles (z-score between − 1.28 to 1.28 SD), which served as the reference group; and large for gestational age (LGA), defined as birth above the 90th percentile (z-score greater than 1.28 SD).

Outcomes: bone quality measurements

The following bone quality measures were automatically calculated from the hip structural analysis from the Lunar Prodigy machine [11]:

- Cross-sectional area (CSA, mm^2): The cross-sectional surface area of the bone excluding regions occupied by marrow or other soft tissues within the pores [33]. CSA is important when it comes to the bone's resistance to compression, and higher values are associated with higher bone strength.
- Cross-sectional moment of inertia (CSMI, mm^4): Measures how the bone mass is distributed around its axis and, like CSA, it is also a predictor of the bone's resistance to bending. The CSMI is expressed as follows:

$$\mathrm{CSMI} = \left(\frac{\pi}{4}\right)\mathrm{x}\ (R^4 - R^4)$$ [34]

R_0 outer radius (the distance from the center to the outer edge of the bone cross-section)

R_i inner radius (the distance from the center to the inner edge, used in the case of a hollow bone structure)

- Hip axis length (HAL, mm): The distance from the base of the greater trochanter to the inner pelvic rim, and a longer HAL is associated with increased fracture risk [14].

- Buckling ratio (BR): Calculated by dividing the width of the femoral neck by the mean cortical thickness [35]. It is a measure for assessing the structural stability of the bone and determining how likely the femoral neck is to buckle (collapse) under stress. A higher BR is associated with an increased risk of buckling. BR is expressed as:

$BR = \frac{R_0}{t}$ [34]

R_0 outer radius

t cortical thickness

These four measures were grouped into two categories: CSA and CSMI, representing bone strength and mass distribution, and BR and HAL, reflecting structural vulnerability and geometry.

Covariates

Potential confounders included sex, birth year, age at bone densitometry, and gestational length. Bone geometry parameters have been shown to be dependent on skeletal size, and for this reason, the models were adjusted for height [36]. To explore whether the associations between birth characteristics and bone quality indicators reflect direct effects independent of adult BMD, we conducted a separate analysis where BMD was added to the model. All analyses were conducted in the total sample, with sex included as a covariate, as the sample size was considered too limited to yield reliable estimates when stratified by sex.

Statistical analysis

Descriptive data are presented as means with SD for continuous data, while categorical data are presented as frequencies and percentages. Normal distribution was assessed through visual inspection of histograms, and they were considered approximately normally distributed. Linear regression analysis was conducted to explore the association between birth characteristics (birthweight, birth length, and birth weight relative to gestational age and sex) and bone quality measures (HAL, CSA, CSMI, and BR). Results are presented as coefficients for both crude and adjusted models, with corresponding 95% confidence intervals (CI). All outcomes were adjusted for sex (categorical), birth year (continuous), age at bone densitometry (continuous), and gestational length (continuous in days). BR and HAL were additionally adjusted for adult height measured at the time of bone densitometry in HUNT in the main model. All models were in separate analyses adjusted for BMD. An additional univariate correlation analysis using Pearson's coefficient was performed to explore the relationship between BR and HAL and BMD.

All statistical analyses were performed using Stata 18.0 (StataCorp LLC, College Station, TX, USA).

Ethics

Participants in HUNT3 and HUNT4 gave written, informed consent for the data to be used for research, including a linkage with other registers. The study was approved by the Regional Committee for Medical Research Ethics, Central Norway (application number 246732).

Results

A total of 2,680 participants aged 20–54 years with bone quality measurements from HUNT3 or HUNT4 were included in the study; of these, 60% were women. Regarding birth characteristics, 3.9% of the participants were born with LBW, and 12.1% were born SGA. The mean maternal age at delivery was 25.9 years (SD 5.1). See Table 1.

The mean age at the time of DXA was 32.7 years (SD 7.5). The mean values for bone quality measurements were CSA 167.7 (SD 30.2) mm^2, CSMI 14.00 (SD 5.25) mm^4, BR 3.49 (SD 1.67), and HAL 112.6 (SD 10.3) mm (Table 1).

Birth weight was positively associated with bone strength measures. For instance, mean CSA ranged from 160.4 mm^2 in the <2.5 kg group to 178.6 mm^2 in the ≥ 4.0 kg group. Similar trends were observed for CSMI (with corresponding values 12.55 to 16.06 mm^4), BR (3.21 to 3.71), and HAL (109.3 to 116.8 mm).

Bone strength indicators: cross-sectional area and cross-sectional moment of inertia

We found a positive association between birth weight, birth length, and birth weight relative to gestational age and sex and CSA (Table 2). After adjusting for sex, birth year, age at DXA, and gestational length, the associations were attenuated but remained statistically significant. Specifically, for every SD increase in birth weight and birth length, CSA increased by 4.33 mm^2 (95% CI: 3.28, 5.37) and 4.29 mm^2 (95% CI: 3.22, 5.36), respectively.

The mean CSMI was 14.0 mm^4 (SD 5.25) (Table 1). We found a positive association between birth characteristics and CSMI (Table 2). After adjustment for sex, birth year, age at DXA, and gestational length, CSMI increased by 0.74 mm^4 (95% CI: 0.58, 0.89) for every SD increase in birth weight, and by 0.45 mm^4 (95% CI: 0.59, 0.91) for every SD increase in birth length. Additionally, participants classified

Table 1 Characteristics of the participants at birth (1967–1997), at baseline HUNT3 (2006–2008) or HUNT4 (2017–2019) and maternal characteristics according to birth weight

Characteristics at birth	All	Birth weight, kg				
		< 2.5	2.5–2.9	3.0–3.4	3.5–3.9	≥ 4.0
No. of participants (%)	2680	106 (4.0)	186 (6.9)	786 (29.3)	1200 (44.8)	402 (15.0)
Small for gestational age n (%)[a]	324 (12.1)	76 (71.7)	122 (65.6)	126 (16.0)	-	-
Appropriate for gestational age n (%)[b]	2117 (79.0)	28 (26.4)	63 (33.9)	656 (83.5)	1174 (97.8)	196 (48.8)
Large for gestational age n (%)[c]	239 (8.9)	2 (1.9)	1 (0.5)	4 (0.5)	26 (2.2)	206 (51.2)
Birth length < 47 cm, *n* (%)	114 (4.3)	73 (68.9)	36 (19.4)	4 (0.5)	1 (0.1)	-
Birth length 47–53 cm, *n* (%)	2326 (86.8)	30 (28.3)	148 (79.6)	777 (98.9)	1137 (94.8)	234 (58.2)
Birth length > 53 cm, *n* (%)	240 (9.0)	3 (2.8)	2 (1.1)	5 (0.6)	62 (5.2)	168 (41.8)
Characteristics at participation in HUNT						
Female, *n* (%)	1596 (59.6)	69 (65.1)	125 (67.2)	506 (64.4)	707 (58.9)	189 (47.0)
First bone densitometry at HUNT3, *n* (%)	2245 (83.8)	93 (87.7)	147 (79.0)	656 (83.5)	1,013 (84.4)	336 (83.6)
Age, mean (SD) years	32.7 (7.5)	31.9 (7.5)	33.1 (7.6)	33.1 (7.6)	32.8 (7.4)	32.0 (7.3)
Height, mean (SD) cm	172.4 (9.0)	168.6 (9.5)	168.4 (8.5)	170.7 (8.9)	172.9 (8.5)	177.3 (8.8)
Weight, mean (SD) kg	78.7 (16.6)	77.7 (18.5)	73.8 (16.8)	76.5 (16.3)	78.8 (15.7)	85.0 (17.6)
BMI, mean (SD) kg/m^2	26.4 (4.9)	27.2 (5.3)	25.9 (5.1)	26.2 (4.9)	26.3 (4.7)	27.0 (5.2)
Current smokers, *n* (%)	329 (12.4)	10 (9.6)	25 (13.6)	89 (11.4)	140 (11.8)	65 (16.3)
Lung symptoms *, *n* (%)	969 (36.3)	50 (47.2)	75 (40.3)	298 (38.0)	400 (33.5)	146 (36.5)
Cross-sectional area (CSA), mean (SD) (mm^2)	167.7 (30.2)	160.4 (29.5)	159.6 (28.2)	163.1 (30.2)	169.0 (29.3)	178.6 (30.8)
Cross-sectional moment of inertia (CSMI), mean (SD) (mm^4)	14.00 (5.25)	12.55 (4.91)	12.29 (4.34)	13.24 (5.23)	14.21 (5.12)	16.06 (5.51)
Buckling ratio (BR), mean (SD)	3.49 (1.67)	3.21 (1.62)	3.34 (1.49)	3.40 (1.61)	3.54 (1.74)	3.71 (1.66)
Hip axis length (HAL), mean (SD) (mm)	112.6 (10.3)	109.3 (10.2)	109.3 (9.4)	111.2 (10.3)	113.0 (10.0)	116.8 (10.5)
Maternal characteristics						
Primiparous, *n* (%)	1,078 (40.2)	52 (49.1)	76 (40.9)	374 (47.6)	449 (37.4)	127 (31.6)
Maternal age years, mean (SD)	25.9 (5.1)	26.3 (5.8)	26.4 (5.2)	25.3 (4.9)	25.9 (5.1)	26.9 (5.2)
- ≤ 19, *n* (%)	199 (7.4)	5 (4.7)	12 (6.5)	73 (9.3)	85 (7.1)	24 (6.0)
- ≥ 35, *n* (%)	151 (5.6)	12 (11.3)	10 (5.4)	32 (4.1)	68 (5.7)	29 (7.2)

[a] Birth weight < 10th percentile

[b] 10th–90th percentile

[c] > 90th percentile

*Includes a wide range of self-reported respiratory symptoms, ever diagnosis of asthma or chronic obstructive pulmonary disease, or use of asthma medication

as LGA had a higher mean CSMI compared to those born AGA or SGA.

Bone geometry indicators: buckling ratio and hip axis length

In the crude analysis, we found significant associations with birth characteristics and BR. After adjusting for relevant confounders, these associations were no longer statistically significant (Table 2).

We found a positive association between birth weight and HAL (Table 2). After adjusting for relevant covariates, HAL increased by 0.29 mm (95% CI: 0.04, 0.55) for every SD increase in birth weight. No significant associations were observed between HAL and other birth characteristics after adjustment (Table 3).

Impact of BMD adjustment on associations with bone quality

To assess the degree to which the observed associations between birth characteristics and bone quality measures were independent of BMD, all analyses were repeated with BMD included as an additional covariate (Table 4). This led to a general attenuation of effect estimates for CSA and CSMI. For example, the association between birth weight (per SD increase) and CSA decreased from 4.33 mm^2 to 1.90 mm^2, while the association with CSMI decreased from

Table 2 Associations between birth characteristics and bone strength indicators, cross-sectional area (CSA) and cross-sectional moment of inertia (CSMI) among participants aged 20–54 years with bone densitometry in HUNT3 (2006–2008) or HUNT4 (2017–2019)

Variables	Cross-sectional area (mm^2) (N = 2648)		Cross-sectional moment of inertia (mm^4) (N = 2648)	
	Crude mean difference	Adjusted mean difference* (95% CI)	Crude mean difference	Adjusted mean difference* (95% CI)
Birthweight				
Continuous (per 100 g)	1.07	0.80 (0.61, 1.00)	0.20	0.14 (0.11, 0.16)
Continuous (per SD)[a]	5.76	4.33 (3.28, 5.37)	1.08	0.74 (0.58, 0.89)
Birth length				
Continuous (per cm)	2.70	1.84 (1.38, 2.31)	0.55	0.32 (0.26, 0.39)
Continuous (per SD)[b]	6.26	4.29 (3.22, 5.36)	1.27	0.45 (0.59, 0.91)
Birth weight relative to gestational age and sex[c]				
Small for gestational age (SGA)	−5.28	−4.13 (−7.03, −1.22)	−1.25	−1.03 (−1.46, −0.61)
Appropriate for gestational age (AGA)	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Large for gestational age (LGA)	6.41	6.34 (2.94, 9.73)	1.05	1.13 (0.62, 1.63)

*Adjusted for sex, birthyear, age at DXA and gestational length

[a] 1 standard deviation (SD) increase in birthweight = 536.6 g

[b] 1 standard deviation (SD) birth length = 2.3 cm

[c] SGA = birth weight < 10th percentile; AGA = 10th–90th percentile; LGA = > 90th percentile

Table 3 Associations between birth characteristics and bone geometry indicators buckling ratio (BR) and hip axis length (HAL) among participants aged 20–54 years with bone densitometry in HUNT3 (2006–2008) or HUNT4 (2017–2019)

Variables	Buckling ratio (N = 2646)		Hip axis length (mm) (N = 2512)	
	Crude mean difference	Adjusted mean difference* (95% CI)	Crude mean difference	Adjusted mean difference* (95% CI)
Birthweight				
Continuous (per 100 g increase)	0.02	0.01 (−0.01, 0.02)	0.38	0.05 (0.01, 0.10)
Continuous (per SD increase)[a]	0.11	0.04 (−0.04, 0.11)	2.06	0.29 (0.04, 0.55)
Birth length				
Continuous (per cm increase)	0.06	0.01 (−0.02, 0.04)	1.16	0.03 (−0.09, 0.15)
Continuous (per SD increase)[b]	0.13	0.02 (−0.06, 0.09)	2.69	0.07 (−0.20, 0.34)
Birth weight relative to gestational age and sex[c]				
Small for gestational age (SGA)	−0.20	−0.10 (−0.29, 0.09)	−2.46	−0.13 (−0.82, 0.56)
Appropriate for gestational age (AGA)	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Large for gestational age (LGA)	0.04	−0.02 (−0.24, 0.21)	2.16	0.42 (−0.38, 1.22)

*Adjusted for sex, birthyear, age at DXA, gestational length, and height at HUNT participation

[a] 1 standard deviation (SD) increase in birthweight = 536.6 g

[b] 1 standard deviation (SD) birth length = 2.3 cm

[c] SGA = birth weight < 10th percentile; AGA = 10th–90th percentile; LGA = > 90th percentile

0.74 mm^2 to 0.55 mm^2 (Table 4). Despite the attenuation, the estimates remained relatively consistent.

For BR, the associations with birth characteristics became stronger and more consistent after BMD was added to the model. For example, the association for birth length, which had attenuated in the adjusted model, returned to the same level as in the crude analysis once BMD was included. Similarly, participants born SGA consistently showed lower BR compared to those born AGA in both the crude and BMD-adjusted models, while this association appeared less consistent in the adjusted model without BMD.

A univariate correlation analysis revealed a clear negative correlation between BMD and BR ($r = -0.24$, $p < 0.001$), indicating that individuals with higher BMD tend to have lower BR values. This supports the interpretation that BMD

Table 4 Associations between birth characteristics and bone quality measures among participants aged 20–54 years with bone densitometry in HUNT3 (2006–2008) or HUNT4 (2017–2019), after adding BMD to the main adjusted model. All presented as adjusted mean difference

Variables	Cross-sectional area	Cross-sectional moment of inertia	Buckling ratio	Hip axis length
Birthweight				
Continuous (per 100 g increase)	0.35 (0.26, 0.45)	0.10 (0.08, 0.13)	0.01 (−0.01, 0.20)	0.05 (0.01, 0.10)
Continuous (per SD increase)[a]	1.90 (1.38, 2.43)	0.55 (0.41, 0.68)	0.13 (0.07, 0.20)	0.29 (0.04, 0.55)
Birth length				
Continuous (per cm increase)	0.92 (0.69, 1.15)	0.25 (0.19, 0.31)	0.06 (0.03, 0.09)	0.03 (−0.09, 0.15)
Continuous (per SD increase)[b]	2.13 (1.60, 2.66)	0.58 (0.44, 0.72)	0.13 (0.06, 0.20)	0.07 (−0.20, 0.34)
Birth weight relative to gestational age and sex[c]				
Small for gestational age	−3.06 (−4.51, −1.61)	−0.95 (−1.33, −0.57)	−0.07 (−0.25, 0.11)	−0.13 (−0.82, 0.55)
Appropriate for gestational age	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Large for gestational age	2.37 (0.68, 4.06)	0.81 (0.37, 1.26)	0.02 (−0.19, 0.23)	0.42 (−0.39, 1.22)

*Adjusted for sex, birth year, age at DXA, and gestational length (identical to the main adjusted model), with BMD at the femoral neck added as an additional covariate. Buckling ratio and Hip axis length models were additionally adjusted for height at HUNT participation

[a] 1 standard deviation (SD) increase in birthweight = 536.6 g

[b] 1 standard deviation (SD) birth length = 2.3 cm

[c] SGA = birth weight < 10th percentile; AGA = 10th–90th percentile; LGA = > 90th percentile

may mask structural differences in BR when not accounted for in the model.

For HAL, further adjustment for BMD did not change the associations with birth characteristics. The estimates remained stable, suggesting that the relationship between birth weight and HAL is not influenced by BMD.

Discussion

In this large, population-based cohort of adults aged 20–54 years (mean age 34 years), we found positive associations between birth characteristics and DXA-derived indicators of bone quality. The associations were strongest and most consistent for bone strength measures (CSA and CSMI), while associations with bone geometry (BR and HAL) were weaker and less consistent. To our knowledge, this is the first study to explore the association between birth characteristics and bone quality indicators in young adults, offering new insights into how early-life factors may influence bone quality later in life.

While BMD has long been the primary focus in assessing bone health, our findings suggest that structural parameters provide additional and complementary information about skeletal strength. Notably, most associations remained significant after adjusting for BMD, supporting that birth characteristics influence bone quality through mechanisms that are, at least partly, independent of BMD.

The bone quality measures used are automatically derived from standard DXA scans and do not require additional procedures, making them readily available for clinical use without extra cost or patient burden.

Previous research has shown that early growth, measured by weight at one year of age, is associated with CSMI in adulthood [24]. In addition, studies have demonstrated that bone quality measures predict hip fracture risk in addition to conventional BMD at the femoral neck in postmenopausal women [13–15], and for HAL in premenopausal women [16]. Specifically, lower CSA and CSMI, along with higher BR and longer HAL, have been associated with increased fracture risk, highlighting the clinical relevance of these bone quality indicators.

Interestingly, our findings revealed a paradoxical pattern regarding the influence of birth characteristics on bone geometry: while higher birth weight was associated with greater CSA and CSMI, both indicators of stronger and more robust bone structure, it was also associated with longer HAL and increased BR, which have been linked to increased fracture risk. This apparent contradiction may be explained by the fact that the different bone quality measures represent distinct aspects of bone health. Whereas CSA and CSMI reflect the mechanical strength and resistance to loading, HAL and BR are more indicative of bone geometry and structural vulnerability.

The associations between birth characteristics and BR became stronger and more consistent after adjusting for BMD. This suggests that there is a direct link between birth characteristics and BR, but part of this link may be hidden because some of the effects are mediated through BMD.

Moreover, HAL has been shown to be strongly linked to genetic factors, with heritability estimates as high as 80%, independent of body composition and height [37]. This suggests that some aspects of bone geometry may be less modifiable by early-life exposures but rather determined by inherited traits. Together, these findings highlight the importance of assessing both bone strength and bone geometry when evaluating fracture risk, as they may reflect different but complementary dimensions of skeletal integrity.

CSA and CSMI were most influenced by BMD adjustment, likely because higher BMD typically reflects more mineralized bone mass in the cross-section. In contrast, BR and HAL were less affected by BMD, as they primarily represent bone geometry and shape rather than mineral content. However, the univariate correlation analysis revealed a negative correlation between BR and femoral neck BMD, indicating that higher BMD could mask structural differences in BR when not accounted for. This aligns with the understanding that bones with higher mineral density are structurally more robust and less prone to buckling. HAL, on the other hand, showed only a weak positive correlation with BMD, indicating that it is largely independent of mineral density and may represent a distinct geometric trait.

However, more knowledge is needed on how to interpret and apply this information in clinical settings. Previous studies suggest that, in addition to BMD, certain bone quality measures such as CSA and CSMI may be modifiable through mechanical loading and physical activity. For example, a study comparing young adult female handball players to inactive women found significantly higher femoral neck BMD and CSMI among the athletes (24). Similarly, former middle-aged basketball players demonstrated higher CSA and CSMI compared to inactive peers, suggesting long-term benefits of high-impact physical activity on bone quality measures (25). Further, a study of elite male athletes showed that runners and gymnasts had significantly greater CSA and CSMI compared to swimmers and non-athletic controls, despite similar BMD values, highlighting the added value of geometric indices in assessing bone strength [38]. These findings underscore the potential for targeted exercise interventions to improve bone quality in a similar way to what has been shown for BMD.

Strengths of this study include the large sample size and the use of high-quality, registry-based birth data, which exclude the risk of recall bias and enhance the validity of the exposure variables. It is the first study that examines the relationship between birth characteristics and bone quality measures in young adults. However, there are some limitations to consider when interpreting the results. Hip structural analysis variables derived from DXA scans should be interpreted with some caution due to known limitations in measurement precision [39]. This is particularly relevant for variables such as BR and HAL, which are sensitive to limb position and selection of regions of interest. Although standardized procedures were followed and trained staff conducted the DXA examinations in the HUNT study, we cannot completely rule out the possibility of measurement variability affecting these outcomes. However, such variability is likely random and unrelated to birth characteristics, and therefore unlikely to have introduced systemic bias in the observed associations. Moreover, the larger sample size in our study helps to mitigate this limitation by reducing the impact of random measurement error and increasing the reliability of the observed association at the population level. A total of 247 participants had right hip measurements used for HAL where left hip data was missing. Previous DXA studies have demonstrated that hip axis length shows high left–right correlation and statistical equivalence, with no significant side to side differences detected [40]. We did not perform sex-stratified analyses due to limitations in sample size, particularly within subgroups such as individuals born with low birth weight, as this would have reduced the statistical power to detect meaningful associations. This limitation should be considered when interpreting potential sex-specific patterns, and future studies with larger sex-stratified samples will be important to address these questions.

In conclusion, our findings suggest that birth characteristics, particularly birth weight and length, are associated with both bone strength and geometry in young adulthood. These associations underscore the importance of early-life factors in skeletal health and highlight the potential of DXA-derived bone quality measures as complementary tools in evaluating bone strength. Future research should explore the mechanisms underlying these associations and assess their relevance for fracture risk prediction and preventive strategies. Further studies are needed to confirm these findings and examine how early-life factors may interact with modifiable lifestyle behaviors throughout the life course.

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Data Availability The data that support the findings of this study are derived from the Trøndelag Health Study (The HUNT Study). Due to Norwegian privacy legislation and participant consent restrictions, HUNT data cannot be shared publicly. Researchers may, however, obtain access to the data by submitting an application to the HUNT Data Access Committee (DAC). Access is granted only for approved research projects and requires appropriate ethical approval. Information about available data, application procedures, and access requirements is provided by the HUNT Research Centre and can be found at the offi cial HUNT data access page: https://www.ntnu.edu/hunt/data/

Declarations

Conflicts of interest None.

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