Bone Mineral Density and Dickkopf-1 in Adolescents with Non-deletional Hemoglobin H Disease

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Abstract

Background: Low bone mineral density (BMD) is prevalent in individuals with β-thalassemia which might be related to increased circulating dickkopf-1 (Dkk-1). These data are limited in α-thalassemia. **Objectives:** To evaluate the prevalence of low BMD in adolescents with non-deletional hemoglobin (Hb) H disease. Additionally, we aimed to examine the association between serum Dkk-1 concentration and BMD. **Methods:** Participant medical records were reviewed. The lumbar spine (LS) and total body (TB) BMD were measured and converted into height-adjusted z-scores. Serum Dkk-1, osteocalcin and C-telopeptide of type-I collagen (CTX) concentrations were also analyzed. **Results:** Thirty-seven participants (59% female, 86% Tanner stage [?]2, 95% regularly transfused) had mean age 14.6 ± 3.2 years, and average pretransfusion Hb and ferritin concentrations of 8.8 ± 1.0 g/dL and 958 ± 513 ng/mL, respectively. No participants had experienced fracture. The prevalence of low LSBMD and TBBMD was 42% and 17%, respectively. LSBMD z-score was lower in males vs. females (p-value = 0.029). LSBMD and TBBMD z-scores were correlated positively with BA, Tanner stage, and BMI, and negatively with Dkk-1 (p-values <0.05). Dkk-1 was correlated positively with history of delayed puberty, and negatively with transfusion interval (p-values = 0.038). Osteocalcin and CTX did not correlate with BMD or Dkk-1. Multiple regression analysis showed Dkk-1 inversely associated with TBBMD z-score adjusting for confounders (p-value = 0.009). **Conclusions:** We demonstrated a high prevalence of low BMD in adolescents with non-deletional Hb H disease. Moreover, Dkk-1 inversely associated with TBBMD suggesting it may serve as bone biomarker in thalassemia.

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Running title: Bone mass and dickkopf-1 in α-thalassemia

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Abbreviations	**Full terms**
25OHD	25-hydroxy vitamin D
β-TI	β-thalassemia intermedia
β-TM	β-thalassemia major
BA	Bone age
BMD	Bone mineral density
BMI	Body mass index
CS	Constant Spring
CTX	C-terminal telopeptide of type-I collagen
Dkk-1	Dickkopf-1
Hb	Hemoglobin
IGF-1	Insulin-like growth factor-1
LIC	Liver iron concentration
LS	Lumbar spine
OC	Osteocalcin
RANK	Receptor activator of NF-kB
TAO	Thalassemia-associated osteoporosis
TB	Total body
TSH	Thyroid-stimulating hormone
USTCRN	United States Thalassemia Clinical Research Network