

## Cross Sectional Observational Study of Osteoporosis in Thalassemia

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### Synopsis:

Beta Thalassemia Major ( $\beta$  TM) is associated with characteristic bone deformities that are considered the result of continuous massive ineffective erythropoiesis. These abnormalities resolve with regular transfusions starting early in life. Despite current management, there is growing awareness that adults with  $\beta$  TM frequently manifest low bone mass and complain of bone pain. However, little is known about the presence of bone disease in other Thalassemia syndromes, current rates of fractures and associations with low bone density. Presence of bone disease in children and adolescents is unclear, and furthermore, the factors that may affect bone mass and fractures remain poorly defined.

The Thalassemia Clinical Research Network (TCRN) comprises five of the larger Thalassemia centers in North America. All TCRN patients regardless of Thalassemia genotype, age 6 and older, with no pre-existing medical condition requiring steroids, were asked to participate. Bone mineral density (BMD) of spine and total hip and total body bone mineral content (BMC) were measured by Dual Energy x ray Absorptiometry (DXA). Vertebral abnormalities were assessed by morphometric x ray absorptiometry (MXA). Medical history was obtained by patient interview and review of medical records. Participants underwent a complete physical examination and a blood and urine collection.

In all, 370 subjects, 181 males (49%), 189 females (51%), mean age 22.9 yrs (range 6.1 to 75.4 yrs) were studied. A high prevalence of low lumbar and hip BMD was found across all Thalassemia syndromes. Overall, lumbar and hip BMD  $z < -2$  was seen respectively in 46.2% and 24.9% of all participants. Age, weight Z score and presence of hypogonadism were found to be the strongest negative predictors of spine and hip BMD and total body BMC. There was a steep decline in BMD during adolescent years and peak bone mass was sub-optimal. Treatment of hypogonadism was found to have no effect on BMD. The overall rate of fractures was 35%. Bone pain the 30 days prior to this study was reported by 34% of all participants. BMD was negatively associated with fractures (odd ratio for lumbar and hip BMD). MXA revealed a large number of vertebral growth plate abnormalities, which were negatively associated with early treatment with the iron chelator, desferoxamine. Finally, markers of bone turnover and serum concentrations of 25 vitamin D correlated negatively with spine and hip BMD, total body BMC and fractures. High rates of vitamin D deficiency (11.9%) and insufficiency (69.5%) were found among all Thalassemia syndromes.

Bone disease in the form of low BMD, frequent fractures and bone pain occur frequently today among patients with all Thalassemia syndromes. Childhood and adolescence appear to be critical periods because of significant decrease in BMD during this time and sub-optimal peak bone mass. Low BMD is associated with the presence of hypogonadism, regardless of gonadal steroid replacement, and increased risk for fractures.