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**Impact of iron deficiency on hemoglobin A2% in obligate β-thalassemia heterozygotes**

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**Abstract**

**Introduction:**The potential impact of concomitant iron deficiency on hemoglobin A2 (HbA2)-based identification of β-thalassemia trait (βTT) is a worrisome issue for screening laboratories. This is especially true for resource-constrained settings where iron deficiency is widespread and molecular confirmatory tests for borderline low HbA2 values may be unavailable.

**Methods:**Obligate βTT carrier individuals (n = 752) were identified during screening studies on the parents of thalassemia major patients. HbA2%, complete blood counts and serum iron, ferritin and transferrin saturation were studied. Iron-deficient individuals (n = 135) with normal range HbA2% were taken as controls.

**Results:**Concomitant iron deficiency (defined as ferritin ≤15 ng/mL and/or transferrin saturation ≤15%) was present in 20.7% (156/752) βTT cases, that is, 33.3% females (122/366) and 8.8% males with βTT (34/386). Mean HbA2 in iron-replete βTT was 5.4 ± 0.8 (range 3.1-7.9) and in iron-deficient βTT was 5.4 ± 0.9 (range 3.3-7.6). HbA2 < 4.0% was found in 23/752 (3.1%) βTT: 13/595 iron-replete (2.2%) and 10/157 (6.4%) iron-deficient βTT individuals. However, five of the 10 iron-deficient βTT cases carried the silent CAP+1 (A>C) β-thalassemia allele accounting for the borderline HbA2%. On a separate analysis, all five severely anemic βTT (Hb < 80 g/L) and 16/17 βTT with severe hypoferritinemia (<5 ng/mL) had HbA2 > 4.5%. The single case with serum ferritin 4.8 ng/mL and HbA2 3.3% showed a CAP+1 (A>C) mutation.

**Conclusions:**Iron deficiency was prevalent among north Indian βTT individuals, especially women. After adjusting for other causes of low HbA2 in βTT, iron deficiency, even when very severe, was very unlikely to interfere significantly with HbA2-based identification of βTT.

**Keywords:**Thalassemia screening; hemoglobin A2; heterozygous β-thalassemia; iron deficiency; microcolumn chromatography; screening.

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