Letter to the Editor

Mutational spectrum of thalassemias in India

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Sir,

Thalassemias are common genetic disorders in the Indian subcontinent.[1] Thalassemia major is the severe phenotype which requires lifelong transfusions and bone marrow transplantation is the only curative option available. Knowledge of the ethnic and geographic origin would enable molecular analysis to be tailored, keeping in view the specific mutations in that community or area. The following write-up gives a concise representation of the common thalassemia mutations in Indians.

Beta-thalassemia is clinically more significant in India, with higher incidence in certain communities. Few common mutations account for >95% of severe beta-thalassemia cases. Concurrent presence of alpha thalassemia modifies the phenotype of beta-thalassemia. Alpha-thalassemia is not a significant problem in India because the severe alpha deletion mutations are less common in this region. The carrier rate for β-thalassemia varies from 3-17%.[1] The alpha thalassemia carrier rate in India varies from 1 to 80%.[1] But it is clinically less significant than β-thalassemia. Alpha thalassemia if present in β-homozygous thalassemia patients ameliorates the phenotype and majority present as thalassemia intermedia.[2,3] Hb E (hemoglobin E) is abnormal hemoglobin prevalent in North-Eastern States.[4]

The five common mutations -IVS 1-5 G → C, IVS 1 -1 G → T, Codon 41/42 (- TCTT), Codon 8/9 and the 619 bp deletion account for over 90% of the mutations in β-thalassemia patients.[5,6] The mutations reported from different regions of India are listed in Figure 1.[7-12] IVS-I-5 (G → C) is the most common beta-thalassemia allele in the Indian population. Sindhis and Lohanas especially from Gujarat show high prevalence of the 619 bp deletion mutation. Rare beta-thalassemia mutations were found in 87/1233(7.06%) carriers.[8] High frequency of the IVS-1-1 (G →T) mutation was also found in Sindhis (25.5%), Punjabi Hindus (34.7%) and Lohanas (31.2%) in the study. Jat Sikhs, a subcaste of Punjabis, revealed a very high prevalence (46%: 41/88) of the mild β++ promoter

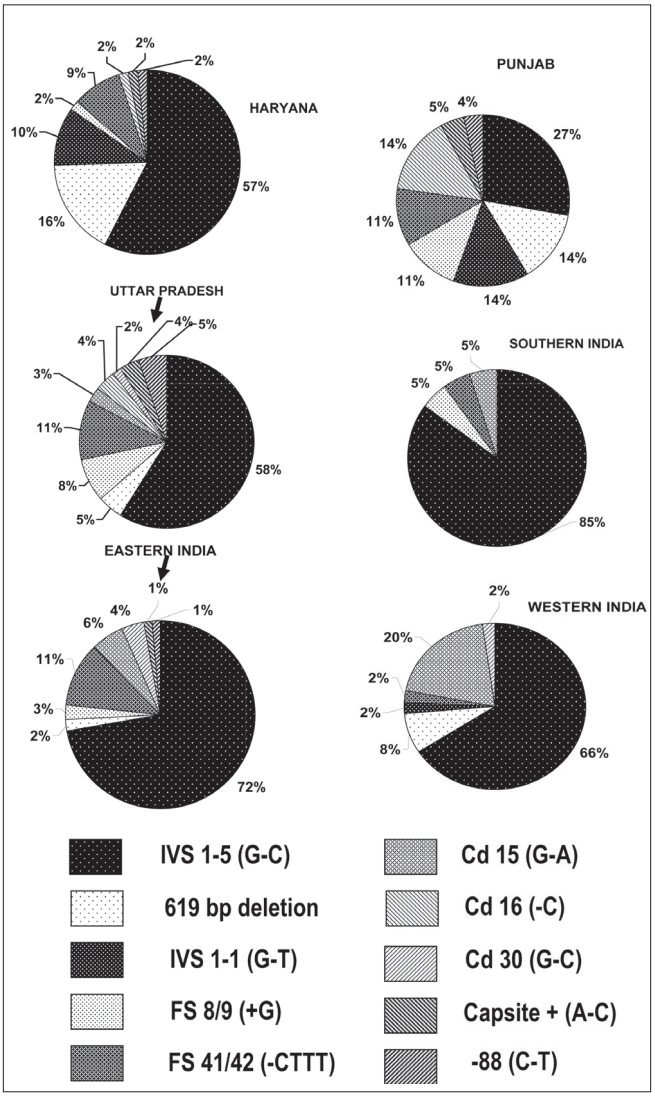

Figure 1: The pie charts depict the prevalence of ten common mutations in β-thalassemia cases in different regions of India. The keys are given as shaded rectangles

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mutation -88 (C-T) in a recent study.[13] Un-transfused patients had characteristically high Hb F (38.1-68.6%, mean 47.4%) and also Hb A2 (5.7-9.8%, mean 6.88%) values.

In alpha thalassemia the common mutations are - $\alpha^{3.7}$, - $\alpha^{4.2}$, - ^{SA} (South African deletion)[14] and Hb Constant Spring. The commonest mutation is - $\alpha^{3.7}$deletion. Hb Koya Dora is found at high frequency (10%) in certain communities of Andhra Pradesh.[15] Hb Constant Spring and Hb Koya Dora are termination codon mutations leading to an elongated alpha chain. The α^0 alleles (double deletion on one chromosome involving 2 alpha genes) are less common in India compared to neighboring South East Asian Countries like China and Taiwan. This is one of the reasons for alpha-thalassemia being a less important problem.

To conclude, knowledge of the native origin of affected families can help in identifying the common possible mutations and accordingly molecular analysis can be phased out.

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