Genetic modifier of Hereditary Haemochromatosis gene (*HFE)* in transfusion dependant thalassaemia: phenotype genotype relationship in a Sri Lankan population

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Abstract

Background and Purpose: Iron overload is a major complication in patients with transfusion dependant thalassaemia and co- existence of Hereditary Haemochromatosis (HH) aggravates this complication. Two common missence mutations in the *HFE* gene 845G>A (p.C282Y) and c.187C>G (p.H63D) are associated with HH. The aim of this study was to genotype c.845G>A and c.187C>G mutations in regularly transfused β thalassaemia patients and to correlate the association between these mutations with their serum ferritin levels.

Method: 125 patients with β thalassaemia who were on regular blood transfusions referred to ward 2, 3, 4 and 9, Lady Ridgway Hospital, Colombo and who were at Thalassaemia center, Teaching Hospital, Anuradhapura were recruited to the study. *HFE* gene was tested for c.845G>A and c.187C>G mutations by Amplification Refractory Mutation System Polymerase Chain Reaction. Serum ferritin level was measured using electrochemiluminescense method. The C-reactive protein (CRP), erythrocyte sedimentation level (ESR), and Serum Glutamine Aspartate Transaminase (SGPT) levels were done to exclude coexisting inflammatory states and liver disease. The results were analyzed using Student's t-test.

Results: None had the *p*.C282Y variant. 23 were heterozygous for the *p*.H63D variant. Allele frequencies of the two variants; *p*.C282Y and *p*.H63D, were 0% and 9.2% respectively. There was no statistically significant difference *(p* = 0.865) between the mean ferritin level of carriers and wild type of the *p*.H63D variant; the levels were 4987ng/ml and 4571ng/ml respectively. CRP, ESR and SGPT were elevated in 9 (7.2%; c.187CC 4, c.187CG 5), 65(52%; c.187CC 50, c.187CG 15), 82(65.6%; c.187CC 64, c.187CG 18) respectively. The confounding effect of

inflammation and liver disease on the serum ferritin level could not be analyzed due to small sample size.

Conclusions: In Sri Lankan patients with transfusion dependant thalassaemia the *p*.C282Y mutation is rare and cannot be considered as a risk factor for iron over load. The *p*.H63D mutation may be a potential risk factor for iron overload; this needs to be verified using larger cohort studies.

Key words: *Hereditary Haemochromatosis (HH), Hereditary Haemochromatosis gene (HFE), thalassaemia patients*