Title: CORRELATION OF GENOTYPE WITH PHENOTYPE IN BETA THALASSAEMIA INTERMEDIA IN SRI LANKA

Abstract Category: Non-Transfusion Dependent Thalassaemia

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ABSTRACT:

Background & Aims
Previous studies have shown that a third of all patients attending thalassaemia centers in Sri Lanka have non transfusion dependant thalassaemia (NTDT); the majority of whom have Hb E β thalassaemia. Previously we attempted to study the genetic basis of non E β thalassaemia intermedia (TI) patients in Sri Lanka. In the present study we aim to correlate their genotype with the phenotype.

Methods
Fifty unrelated TI patients identified from the five main thalassaemia centers were assessed clinically and categorized into "mild", "moderate" and "severe" groups according to their clinical severity. DNA analyses were performed by the standard techniques.

Results
Seventeen patients were homozygous or compound heterozygous for β mutations. Five of the homozygotes who carried two mild β alleles including a rare promoter mutation - 90 C>T, Hb variant alleles of Hb G-Szuhu and Hb G-Coushatta; invariably had mild disease. Nine inherited two severe β alleles with either one or two α gene deletions; despite the α deletions they had severe disease. Out of three individuals who carried two β alleles with normal α gene, one had Xmn I +/+ and had mild disease. We were unable to explain the phenotype in two individuals in this group with the existing genetic data.

Thirty three patients were heterozygous for a β mutation IVSI-5 G>C (n=12) was the commonest. Twenty eight of the heterozygotes carried excess α genes and had a mild to moderate phenotype. In this group of individuals, inherited with single β allele with normal α genes, the genetic studies could not explain the phenotype in five individuals.

Conclusion
The clinical outcomes of our TI population were mostly explained by the genotypes linked to the α and β gene cluster. However, in a minority, the existence of other causative genetic determinants remains to be molecularly defined.