Title: Heterogeneity Of Sever Beta Thalassemia in Pakistan: Prevalence and Implication of XmnI Polymorphism and Alpha Thalassemia

Yasmeen Humaira[1], Layton Mark[3], Killeen Natalie[4], Hasnain Shahida[1,] Foroni Letizia[3,4] and Toma Sarmad[4]

1. Department of Microbiology and Molecular Genetics, University of the Punjab, Quaid-e-Azam Campus, 54590, Lahore, Punjab Pakistan.
2. Department of Microbiology and Molecular Genetics, The Women University, Multan Punjab Pakistan.
3. Centre for Haematology, Department of Medicine, Imperial College London, London, United Kingdom
4. Department of Medicine, Imperial College Healthcare NHS Trust, Hammersmith Hospital, London, United Kingdom

Background: B-thalassemia is a monogenic inherited quantitative blood disorder with considerable heterogeneous clinical manifestations. Several genetic determinants are associated with its phenotypic variability such as HBB and HBA genotyping and fetal hemoglobin (HbF).

Aim
A multicenter study aimed to investigate frequency of HBG2:c.-211C>T base-pair substitution (historically described as -158 GγXmnI polymorphism) among homozygous or compound heterozygous beta thalassemia patients and relationship between beta and alpha genotypes.

Methods
Beta thalassemia patients (n=161) were identified on the ground of haematological parameters, and further screened for mutations of the Alpha (HBA2 and HBA1) and Beta (HBB) Globin genes as well as Gamma (HBG2) Globin gene XmnI polymorphism using PCR based methods. All data were analysed by SPSS software.

Result
The -158 GγXmnI polymorphism was present in 57 (36%) patients in which HBB:c.27_28insG (p.Ser10Valfs*14) was the most common beta-mutation 33 (34.5%). More than half of the patients received first blood transfusion ≤1year (71.5% n=113). In patients with both the alpha globin deletion and XmnI polymorphism, the clinical onset of thalassemia occurred later in life (e.g. 1.8 to 2 years of age). A statistically significant (*p*-value 0.01) relationship was found between XmnI polymorphism and beta thalassemia while no significant association between XmnI polymorphism and FBT was observed.

Conclusion
Heterogeneity in clinical and haematological parameters in thalassemia major show that monogenic disorders can present with a wide spectrum of disease severity. This can be helpful in better prognosis and treatment to ameliorate the disease in the long run.