β-Thalassemia: Prevention in Jordan

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Abstract

β-thalassemia is an autosomal recessive genetic disorder, characterized by defective beta-globin chain synthesis. At a carrier rate of 24%- in a Jordanian population of about 5 million, with no effective treatment available, β-thalassemia represents a major financial and social burden on the patients and their families as well as on the national health system. This is only worsened by the high rate of consanguineous marriages in Jordan, estimated to be between 2030%- (this includes only first-cousin marriages) for marriages contracted after 1980. To try and address this issue and reduce the number of infants born with β-thalassemia, a prenatal diagnosis program was initiated in Jordan in 1996, in collaboration between the National Center for Diabetes, Endocrinology and Genetics and the Gynecology Department at the King Hussein Medical Centre. In total, 324 chorionic villus samples (CVS) were screened for one of the seven most common β-thalassemia mutations in the Mediterranean region, between 19962009-. Although most of the couples requesting the screen already had at least one affected child, in majority of cases, where CVS screen returned positive (i.e. the fetus was affected), the couples opted for selective termination of pregnancy. The initiation of prenatal screening (first of its kind in Jordan) together with the introduction of obligatory premarital screening for β-thalassemia in 2007, are both seen as positive steps towards the reduction and eventual prevention of β-thalassemia in Jordan.

Introduction

Thalassemia occurs when one or more of the disease-related genes fails to produce functional protein, leading to a shortage in one of the four hemoglobin subunits (hemoglobin normally consists of two alpha and two beta subunits) (Figure 1). -thalassemia occurs when an α-globin gene fails (HBAD and/or HBAA), β-thalassemia, characterised by reduced synthesis of the hemoglobin subunit beta, results from different mutations in the hemoglobin β-gene HBB (Panigrahi and Agarwal, 2008; Weatherall and Clegg, 1981). So far, more than 200 mutations of the HBB gene have been characterised (Figure 2), most of them being single point mutations.

Mode of inheritance

β-thalassemia is inherited in an autosomal recessive manner. Provided that the parent and the mutated copy of the HBB gene from the other parent) and chance of being an asymptomatic carrier (inheriting a normal copy from one parent) is 50%. β-thalassemia is inherited in an autosomal recessive manner. Provided that

Conclusion

The development of safe prenatal testing methods for the thalassemia has evolved in Jordan despite an atmosphere of profound ethical, legal and social concerns. Prenatal diagnosis for β-thalassemia was the first preventative genetic service to be set up in Jordan. The PCR-based methods utilized have been found to have a low error rate (0.1%) in comparison with other fetal diagnostic methods such as globin chain synthesis and southern blot analysis. Gene sequencing has also been successfully utilized at NCDEG, in cases where mutations could not be identified using the conventional PCR method. In our service, no misdiagnoses were reported. Implementing the obligatory pre-marital screening together with prenatal diagnosis for β-thalassemia in Jordan are aimed at reducing the rate of occurrence and eventually prevention of β-thalassemia. Continued progress depends on enhanced awareness of prenatal diagnosis and improved access to reproductive genetics services.

Pre Natal Di agnosis

As part of prevention of β-thalassemia in Jordan, a prenatal diagnosis program was initiated in collaboration with the Gynecology Department at the King Hussein Medical Centre. In total, 324 chorionic villus samples (CVS) were screened for one of the seven most common β-thalassemia mutations in the Mediterranean region, between 19962009-. Those mutations included IVSII-1 (G-A), IVSII-110 (G-A), IVSII-745 (C-G), IVSII-6 (T-C), IVSII-1 (G-A), codon 39 (C-T) and codon 37 (G-A). Amplification Refractory Mutation System by Polymerase Chain Reaction (ARMS-PCR) was used in order to test the CVS samples for different mutations. Restriction fragment length polymorphism (RFLP) haplotype analysis was also performed to enable exclusion of maternal contamination in the CVS. Out of 300 couples tested, 71% were consanguineous (1st and 2nd degree relatives). In 25% of CVS cases, the foetus was unaffected whereas 53.5% of foetuses were found to be heterozygous and 13.4% were homozygous affected.

References


Table 1. The summary of the results obtained from the molecular analysis of 324 CVS.

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