Research Article

The prevalence of HBG2 polymorphism among Beta Thalassemia major Children in El Minia Governorate and its correlations with HbF level.

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Abstract
Fetal hemoglobin (HbF) is the major modifier for thalassemia severity. HbF is modulated mainly by three major quantitative trait loci (QTL). One of the SNPs in these loci is HBG2. Thirty seven patients with beta thalassemia major from pediatric hematology unit of Minia University hospital, Minia were investigated by a panel of primers and probes using Polymorphism strip assay (β-Thal Modifier StripAssay) Vienna lab. In our study the frequency of wild CC genotypes were 31 patients (83.8%), 5 patients (13.5%) were heterozygous CT and only 1 patient (2.7%) was homozygous TT. We also reveled significant association between HBG2 and Hb F level in beta thalassemia major patients in Minia governorate children.
Keywords: Fetal hemoglobin, thalassemia, pediatric hematology

Introduction
About 1000 babies are born with β-thalassemia major every year from 1.5 million annual live births[(1)].

Thalassemia is considered as a heterogeneous inherited disorder which is caused by the absence or reduction of β-globin synthesis [(2)].

More than 200 different mutations have been associated with thalassemia [(3)].

Xmn-1 polymorphism which is a result from a C >T base substitution at the-158 position of Gγ globin (HBG2) gene, resides in close proximity to locus control region of β-globin gene (β-LCR), which controls differential expression of β-like globin genes throughout the life [(4)].

Aim of the work
We aimed in this study to assess the presence of XmnI-Gγ single nucleotide polymorphisms at position 158 of HBG2 promotor (rs7482144) in β-thalassemia major patients as one of the quantitative loci trait that influence Hb F.

Patients and methods
This study included 37 transfusion dependent β- thalassemia patients with age range of 2 -18 years, attending the Pediatric Hematology unit in Minia University children hospital.

Study procedure
β-thalassemia polymorphism identification of samples was performed by the reverse dot blot hybridization technique (RDB).

For RDB, a panel of primers and probesusing the beta globin strip assay was used (β-Thal Modifier Strip Assay kit, Vienna lab).

All enrolled Patients were subjected to
A-Clinical assessment

1- Full medical History taking including age, sex, age of starting transfusion, family history of consanguinity and similar conditions in family.
2- Clinical examination including general examination stressing on anthropometric measures plotted on growth charts. Local examination including chest, heart, abdominal, musculoskeletal, joints and neurological examination.

B- Laboratory work including

1- Routine lab investigations:

a-Complete blood count.
b- Liver functions.
c- Renal functions.
d- Serum ferritin.
e- Renal functions.

2- Hb electrophoresis

Results

Clinical and laboratory data of the studied patients were tabulated and statistically analyzed. Results of the present study are shown in tables and figures as follows:

Table (I): The distribution of HBG2 in the studied patients:

	HBG2 (No =37)
Negative	**31 (83.8 %)**
Heterozygous	**5 (13.5 %)**
Homozygous	**1 (2.7 %)**

Figure (1): HBG2 distribution among the studied patients.

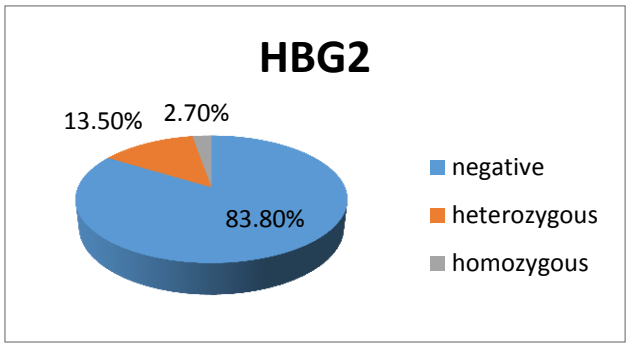

Table (II): HBG2 polymorphism and its correlation with Hb F level.

Hb F level		
Parameter	**Spearman's rho**	**P value**
HBG2	0.388	0.018*

Discussion

Xmn-1 polymorphism is due to C >T base substitution at the-158 position of Gγ globin (HBG2) gene. This polymorphism is presented in close proximity to locus control region of β-globin gene (β-LCR), which controls differential expression of β-like globin genes throughout the life [(4)].

Among 37 patients of β-thalassemia major in the study, the frequency of wild CC genotypes were 31 patients (83.8%), 5 patients (13.5%) were heterozygous CT and only 1 patient (2.7%) was homozygous TT.

In Iran, from 206 β-thalassemia patients with homozygote IVSII-1 mutation, 28 patients (14%) did not show polymorphism (CC), and 178 patients (86%) showed polymorphism either heterozygous CT (44 patients, 21.3%) or TT homozygous (134 patients, 65%)[(4)].

Motovali-Bashi and Ghasemi, (2015) in Iran also found 35 (68.6%) heterozygous (CT) and 16 (31.4%) subjects were homozygous (CC) from 51 patients [(7)].

Numerous studies have revealed that there is a significant positive correlation between the occurrence of T allele at Xmn1polymorphic site and increased amount of HbF. That was shown in French study made on 57 patients, mostly originating from the Mediterranean area and diagnosed as β-thalassemia intermedia[(5)].

Later, this association between HBG2 and high levels of Hb F was found significant in many studies. Roy et al., (2012) was searching for the genetic alterations responsible for high fetal hemoglobin (Hb F) phenotypes in the population of eastern India, they found significant association with HBG2 polymorphism[8].

This also was in another Indian study of Dadheech et al., (2014) in which HbF levels were found to be higher in individuals with the TT genotype followed by CT and CC genotype in β-thalassemia as well as Sickle cell disease patients [9].No association was found between HbF and HBG2 in a study which made on Chinese thalassemia intermedia patients[6].

In our study there was significant positive correlation between HBG2 polymorphism and HbF level (p-value 0.018).

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