
Beta-Thalassemia Mutations in the East of Turkey

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ABSTRACT

This study was planned to determine the frequency of β -thalassemia trait and mutations in Van Lake region, which is in the eastern part of Turkey, surrounded by Iran in the east and by Iraq in the south. This study consist of 1014 healthy students, between the age of 12 and 18 years who are studying in boarding schools in Van city and cities surrounding Van Lake that includes Van, Ağrı, Hakkari, Bitlis, Muş and Siirt. The students were randomly selected according to their school numbers. Their origin was not taken into consideration in selection. Complete blood counts were performed on all donors. The accepted lower limit of mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) were 78 fL and 27 pg respectively. HbA₂ was measured by DE-52 microcolumn chromatography method. β -thalassemia trait with high HbA₂ was found in 6 children. β -thalassemia homozygous form of -30 (T-A) mutation was determined in one child and HbD-Los Angeles heterozygous in another. The β -thalassemia homozygous individual was accepted as two cases in prevalence calculation. We found that the prevalence of β -thalassemia trait was 0.78% in this area. In DNA analyses, there were β -thalassemia gene mutations of FSC 8/9 (+G), -30 (T-A), IVS I-110 (G-A), IVS II-1 (G-A) and IVS I-130 (G-A) in 3, 2, 1, 1 and 1 individuals, respectively. We conclude that although five different β -thalassemia mutation exist in Van Lake region, β -thalassemia is not a potential risk in the east of Turkey.

Key Words: Beta-thalassemia, Turkey, Prevalence.

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INTRODUCTION

Beta-thalassemias (β -thalassemia) are a heterozygous group of autosomal recessive disorders the best available estimate is that approximately 240 million people worldwide are heterozygous for β -thalassemia^[2]. Although there are now more than 180 known β -thalassemia mutation worldwide, each population or

ethnic group usually has a smaller collection of alleles account for the inactivation of the β -globin gene^[1,2].

In Turkey, the prevalence of β -thalassemia carriers is stated to be 2 percent and IVS-I-110, IVS-I-6 mutations are the most common β -gene defects^[3-7]. Because the country has extensive intermingling of ethnically distinct groups, it is expected that the prevalence

of β -thalassemia and distribution of β -thalassemia mutations vary in different regions of Turkey. In this study, we aimed to investigate the prevalence of β -thalassemia carriers and distribution of β -gene mutations in the region surrounding Van Lake, in the eastern part of Anatolia, where the frequency of β -thalassemia was not sufficiently evaluated before.

MATERIALS and METHODS

A total of 1014 healthy students (5 high school and 1 primary school) between the age of 12-18 years old, were selected as target population. The students were attending to boarding schools at Van, originated from five cities around the Lake Van including Van, Hakkari, Bitlis, Siirt, and Muş cities; 505, 158, 133, 115 and 103 students, respectively. The students were selected according to their school numbers. Their origin was not taken into consideration in selection. Sensitivity of mean corpuscular volume (MCV) and mean hemoglobin concentration (MCH) in prediction of β -thalassemia trait were evaluated. The students in whom the levels of hemoglobin (Hb), hematocrit (Hct), MCH and MCV, as measured by electronic cell counters (Coulter-STKS electronic cell counter) were considered for further evaluation. The accepted lower limit of MCV was 78 fL and MCH 27 pg for both sex and age groups. In 108 students who have lower MCV, MCH, serum ferritin levels were measured (using biodpc immulite hormonal otoanalyser). The accepted lower level of ferritin was 10 and 12 ng/mL for 12-15 and 15-18 years age groups, respectively. Twenty-nine students, who have low ferritin levels, were considered to have iron deficiency anemia (IDA). Twenty-eight students whose red blood cell counts were about 5×10^6 /microL and serum ferritin levels were under the limits and 51 students who had normal ferritin levels (total 78 students) were considered for further evaluation. In these patients, the HbA₂ was measured by DE-52 microcolumn chromatography. The high HbA₂ levels (more than 3.5%) were double-checked and in this group HbF levels were calculated by alkaline denaturation technique. The students having high HbA₂ levels were considered to be β -thalassemia carriers. DNA isolation was made as previously described^[8]. Thalassemia mutations were determined by DNA analysis using primers that recognize the most common mutations reported from Turkey^[9,10]. Unidentified samples by this

method were subjected to DNA sequence analysis at Hacettepe University, School of Science^[11].

RESULTS

Among 1014 students, 6 subjects were found to be heterozygote and one subject homozygote for β -thalassemia. The β -thalassemia homozygous individual was accepted as two cases in prevalence calculation. The frequency of β -thalassemia mutation in this study was 0.78%. The FSC-8/9 (+G) mutation was found in 3 unrelated subjects. -30 (T-A) was found in one subject who was homozygous for the mutation. The patient homozygous for -30 (T-A) mutation has had no complaints related to anemia and the diagnosis of thalassemia was made during our survey. There were not any consanguinity for the FSC 8/9 and -30 mutation carriers. Out of IVS I-110 (G-A), IVS I-130 (G-A) and IVS II-1 (G-A) mutations, each was present in 3 different subjects. In one subject, heterozygosity for an abnormal hemoglobin with HbD mobility was detected. HbD was 38.9% of total hemoglobin. Structural analysis revealed that the abnormal Hb was HbD-Los Angeles.

DISCUSSION

β -thalassemia is a common genetic disorder in Turkey and has been studied for several decades by different investigators. The overall prevalence of β -thalassemia trait was found to be 2% in Turkey. However, its frequency varies in different parts of the country. In western, the Mediterranean coast of Turkey, it is the highest (8-10%). The frequency was found to be 0.5-2% in the eastern region of Turkey in previous studies^[12,13]. In our study, the number of the carriers were not sufficient to give any percentages. However, our findings indicated that although β -thalassemia mutations are heterogeneous, the disease is not a potential risk in this region.

Until now, 180 mutations for β -thalassemia were determined worldwide and more than 35 in Turkey. Previous studies in Turkey present the considerable heterogeneity of β -thalassemia mutations among the Turkish population and account for the great variability in clinical expression of this disease. The IVS I-110, IVS I-6 and IVS I-1 mutations are the most common genetic gene defects in whole Turkey^[6, 7,14-16]. In the Lake Van region, however, the commonest genetic defects were found to be FSC 8/9, -30 (T-A), IVS I-110, IVS

I-130 and IVS II-1 mutations. HbD-Los Angeles is the second most common abnormal hemoglobin following HbS in Turkey. Our study indicated that the frequency of β -thalassemia at Van Lake region is lower than the figure given for all over Turkey, as well as the frequency of mutations that are different than the mutation frequency profile given for Turkey. However, no mutation was found to be specific for this region. β -thalassemia mutations were found to be heterogeneous as they were found in other parts of the country. Presence of HbD-Los Angeles shown in a patient in heterozygote state previously in this region (unpublished observation) could be regarded another example for heterogeneity of mutations at β -gene region of hemoglobin.

Heterogeneity of β -thalassemia mutation in a quite small area may be regarded as footprints of many population movements that took place in this area which dated back thousands years ago and continued for many thousands years. Human settlement in Anatolia has been traced back well before 7000 BC. Hittites, Pyrgians, Greeks, Parthians and Mongols established many civilizations. The most decisive influence was the incursion of the Selçuk and Ottomans. Many different ethnic groups have been living in Anatolia for many hundreds years and several genetic elements have been blended during this time. The multiplicity of genetic composition has resulted in the heterogeneity of β -thalassemia mutations in Turkey.

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