

Keywords: Hemoglobinopathy, HPLC, DNA, Sequencing

Anahtar Sözcükler: Hemoglobinopati, HPLC, DNA, Dizileme

Informed Consent: As a result of the explanations, the patients voluntarily asked for the tests to be conducted.

Authorship Contributions

Concept: D.C.; Design: D.C.; Data Collection or Processing: S.D., A.Ç., E.A.; Analysis or Interpretation: D.C., A.Ç., S.C.; Literature Search: D.C., A.Ç.; Writing: D.C., A.Ç.

Conflict of Interest: The authors of this paper have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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Two Rare Pathogenic *HBB* Variants in a Patient with β -Thalassemia Intermedia

Bir Beta Talasemi İntermedya Hastasında İki Nadir Patojenik *HBB* Varyantı

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To the Editor,

The β -thalassemias are a group of hereditary disorders with autosomal recessive inheritance characterized by the presence of defective synthesis of the β -globin chain, an integral component of the hemoglobin molecule, resulting in either partial synthesis (β^+) or complete absence (β^0) [1]. The disease reaches a high frequency in the Mediterranean Basin, Africa, the Middle East, the Indian subcontinent, and Southeast Asia [2]. According to the World Health Organization, the frequency of abnormal hemoglobin is 7% globally [3]. β -Thalassemia major is characterized by completely inhibited synthesis of beta chains [4], and so it must be treated, generally by transfusion therapy [4]. The β -thalassemia major

phenotype has homozygotes or compound heterozygotes for β^0 or β^+ genes. Generally, mutations targeting the coding regions of the gene and conservative regions on the exon-intron boundary lead to β^0 -thalassemia, and mutations in regions that do not encode β^+ -thalassemia. In contrast to the major type, the presence of one normal gene in heterozygotes usually leads to enough normal β -globin chain synthesis so that the affected individuals are usually asymptomatic with only hypochromic and microcytic red blood cells. This condition is referred to as β -thalassemia minor [5]. β -Thalassemia intermedia clinically differs from the major and minor ones with respect to the necessity of transfusion. The degree of anemia for β -thalassemia major is more aggravated than that for β -thalassemia intermedia. The genotype of β -thalassemia intermedia is mostly

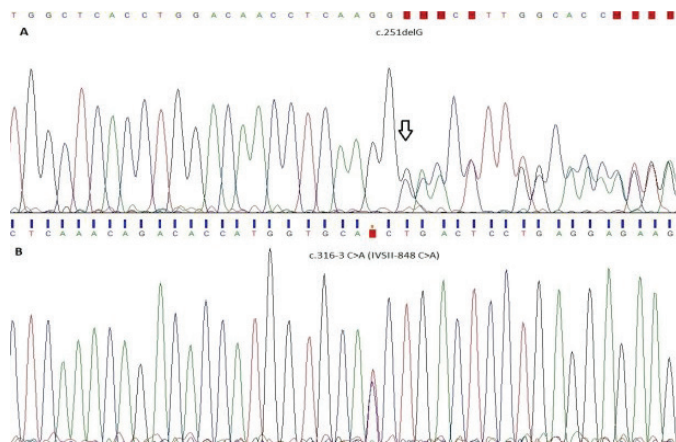


Figure 1. Electropherograms of the patient.

homozygous or compound heterozygous [5]. A 14-year-old male Iraqi patient with Turkish origins presented with infection, mild hepatomegaly, and loss of appetite. Laboratory findings were as follows: white blood cell count, $13.53 \times 10^9/L$; red blood cell count, $3.84 \times 10^{12}/L$; platelet count, $367 \times 10^9/L$; hemoglobin, 7.7 g/dL; hematocrit, 26.3%; mean corpuscular hemoglobin, 22.7 pg; and mean corpuscular volume, 68.5 fL. The patient had no transfusion history. Written informed consent was obtained. A peripheral blood sample was collected in an EDTA-containing tube. Genomic DNA was extracted from the white blood cells. The *HBB* gene was amplified as 2 polymerase chain reaction (PCR) fragments (from the -101 position to the Poly-A signal) using 40 ng of genomic DNA in reaction volumes of 25 μ L. After PCR amplification, sequencing was performed using the BigDye Terminator v3.1 Cycle Sequencing Kit. The patient had heterozygous c.251delG (p.Gly84fs, rs193922555, β^0) and heterozygous c.316-3 C>A (IVSII-848 C>A, rs33913413, β^+) pathologic variants, as shown in Figure 1. Sequencing analysis showed that the father had heterozygous c.251delG and the mother had heterozygous c.316-3 C>A variants. The global frequency of c.251delG and c.316-3 C>A is unknown and 0.00002%, respectively [6]. c.316-3 C>A is observed at a frequency of 0.4% in Turkey [7] and 2.9% in Iraq [8]. c.251delG is observed at 0.2% in Turkey [9] and 10.1% in northern Iraq [10].

These findings may be useful for genetic counseling, premarital/prenatal diagnosis, and prevention programs.

Keywords: Beta thalassemia, *HBB*, Variation

Anahtar Sözcükler: Beta talasemi, *HBB*, Varyasyon

Informed Consent: Written informed consent was obtained from the patient's parents.

Authorship Contributions

Design: V.S.H.; Data Collection: V.S.H., T.F., M.B.; Writing: V.S.H.

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