The First Report of a 290-bp Deletion in \( \beta \)-Globin Gene in the South of Iran

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ABSTRACT

**Background:** \( \beta \)-thalassemia is one of the most widespread diseases in the world, including Iran. In this study, we reported, for the first time, a 290-bp \( \beta \)-globin gene deletion in the south of Iran. **Methods:** Four individuals from three unrelated families with Arabic ethnic background were studied in Khuzestan Province. Red blood cell indices and hemoglobin analysis were carried out according to the standard methods. Genomic DNA was obtained from peripheral blood cells by salting out procedures. \( \beta \)-globin gene amplification, multiplex ligation-dependent probe amplification (MLPA), and DNA sequencing were performed. **Results:** The PCR followed by sequencing and MLPA test of the \( \beta \)-globin gene confirmed the presence of a 290-bp deletion in the heterozygous form, along with -88C>A mutation. All the individuals had elevated hemoglobin A\(_2\) and normal fetal hemoglobin levels. **Conclusions:** This mutation causes \( \beta \)-\( \delta \)-thalassemia and can be highly useful for prenatal diagnosis in compound heterozygous condition with different \( \beta \)-globin gene mutations. **DOI:** [10.18869/acadpub.ibj.21.2.126]

Keywords: \( \beta \)-thalassemia, \( \beta \)-globin gene mutation, Iran, Multiplex ligation-dependent probe amplification

INTRODUCTION

\( \beta \)-thalassemia is one of the most frequent genetic disorders in Iran with a great mutational diversity. More than 280 mutations have been identified in association with \( \beta \)-thalassemia in the country. Mutations are mostly single base substitutions, and in some cases, they may cause deletions or insertions of different regions in a gene\(^{[1,2]}\). \( \beta \)-globin gene deletions, especially those in promoter regions, are usually associated with the high levels of hemoglobin A\(_2\) (HbA\(_2\)) in heterozygous individuals. In addition, the high levels of fetal hemoglobin (HbF) are detected because of \( \delta \)-\( \beta \)-globin gene deletions. However, large deletions of \( \delta \)-\( \beta \)- and \( \gamma \)-globin genes are observed among some carriers with normal levels of HbF. Since most deletions may be missed by DNA sequencing, the identification of deletions in \( \beta \)-globin gene by other means is of great importance\(^{[3,4]}\). In the current study, we detected a 290-bp deletion in four individuals from three unrelated families with Arabic ethnic background in Khuzestan Province, south of Iran.

MATERIALS AND METHODS

The present investigation is a part of a national program for the prevention of thalassemia. In total, four individuals who referred to the Narges Prenatal Diagnostics and Medical Genetics Laboratory (Ahvaz, Iran) during three years participated in this study. The analysis of red blood cell indices and Hb analysis were
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The 290-bp deletion was characterized by DNA sequencing and MLPA test. The mutation removed the region between positions -125 and +78 relative to the β-globin gene mRNA cap site. The MLPA results confirmed the deletion by probes ranging from prob 21 (Promoter) to prob 1 (HBB intron 1) (Fig. 1). Generally, no mutation or deletion was found in the α-globin genes of the studied individuals.

DISCUSSION

The 290-bp deletion was first observed in a Turkish patient and later in many other patients\(^{[8-11]}\). In the present investigation, we reported, for the first time, a 290-bp deletion along with -88C>A mutation in the south of Iran.

The mutation removed the region between positions -125 and +78 relative to the β-globin gene mRNA cap site. According to a previous study\(^{[12]}\), -88C>A mutation allows the β-locus control region to interact with the promoters of δ- and γ-globin genes by competition between fetal and adult globin genes, which result in HbA2 and HbF levels\(^{[12]}\). However, our samples with a 290-bp deletion were just associated with the increased levels of HbA2 and normal HbF.

One of the individuals, offspring of K.B., was a 5-year-old girl, who inherited both defects (290-bp deletion/-88C>A mutation) from her parents. Physical examination of the patient indicated pallor, slight hepatosplenomegaly. The hematological and molecular data of the studied subjects are summarized in Table 1.

### RESULTS

This study reported, for the first time, a 290-bp deletion (c.-176_92+25del) in β-globin gene in four individuals from three unrelated families with Arabic ethnic background in Khuzestan Province. All the individuals had elevated HbA2 and normal HbF levels. The 290-bp deletion was characterized by DNA sequencing and MLPA test. The mutation removed the region between positions -125 and +78 relative to the β-globin gene mRNA cap site. The MLPA results confirmed the deletion by probes ranging from prob 21 (Promoter) to prob 1 (HBB intron 1) (Fig. 1). Generally, no mutation or deletion was found in the α-globin genes of the studied individuals.

### Table 1. The hematological and molecular data of the studied subjects

<table>
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<tr>
<th></th>
<th>S.M.</th>
<th>M.M.</th>
<th>K.B.</th>
<th>Offspring of K.B.</th>
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<tr>
<td>Age (year)</td>
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<td>24</td>
<td>48</td>
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<tr>
<td>Gender</td>
<td>F</td>
<td>M</td>
<td>M</td>
<td>F</td>
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<tr>
<td>Hb (g/dl)</td>
<td>10.9</td>
<td>11.5</td>
<td>12.5</td>
<td>6.4</td>
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<td>RBC (10^5/L)</td>
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<tr>
<td>MCV (fl)</td>
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<td>64.8</td>
<td>66.8</td>
<td>59.3</td>
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<tr>
<td>MCH (pg)</td>
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<td>20.9</td>
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<td>MCHC (%)</td>
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<td>HbA (%)</td>
<td>94.6</td>
<td>92.9</td>
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<td>HbF (%)</td>
<td>0.4</td>
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<td>HbA2 (%)</td>
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<tr>
<td>Origin</td>
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</table>

F, female; M, male; N, normal
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CONFLICT OF INTEREST. None declared.

REFERENCES


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Fig. 1. The chromatogram and histogram of multiplex ligation-dependent probe amplification (MLPA) dosage showing a 290-bp deletion on $\beta$-globin gene. (a) The sequence of a 290-bp deletion presenting in heterozygosity; (b) The histogram of MLPA showing a 290-bp deletion.