REGIONAL MAPPING OF THE GENE FREQUENCY OF $\beta$-THALASSEMIA IN FARS PROVINCE, IRAN DURING 1997-1998.

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ABSTRACT  

Background: The lack of regional mapping data on the gene frequency of thalassemia in province of Fars which is hyperendemic for this disease.  

Objective: To collect regional mapping data on the gene frequency of thalassemia in Fars province, Iran.  

Methods: To evaluate population prevalence of thalassemia minor, all boys attending their final year of high school in Fars province, Iran, were examined. HbA2 levels were measured for boys with a mean corpuscular volume (MCV) of below 80 FL and red blood cell count (RBC) of above 6.1 $^{10^{12}}$L. Individuals with HbA2 levels of higher than 3.5% were considered minor thalassemia. Those with HbA2 levels of lower than 3.5% were treated for two months with oral iron and tests were repeated after this period and a decision was reached using the same algorithm as above. Considering the information on registration sheets, all patients with major thalassemia were contacted and data on sex, age and consanguinity of parents were obtained.  

Results: The frequency of minor thalassemia was 6.88% (95% CI=6.57%-7.2%) in the whole region. The frequency of major thalassemia was 7.2 in 10,000 population (95% CI=6.9-7.5 in 10,000) in the whole region. There was a decrease in prevalence of major thalassemias in the under-10-year-old population. However, this decrease was less significant after adjustment for population age distribution.  

Conclusion: The prevalence of minor and major thalassemia declines in northern regions of Fars province. The relation between the pattern of migration and this map remains a question needing further investigation. The program for the prevention of thalassemia started a decade ago has proved moderately successful. Studying the reasons for the failure of the program and setting up new strategies are recommended.  


Key Words • $\beta$-thalassemia • regional mapping • epidemiology  

Introduction  

The $\alpha$ and $\beta$-thalassemias are the most common inherited single-gene disorders in the world with the highest prevalence in areas where malaria was or still is endemic.  

The burden of this disorder in many regions is of such a magnitude that it represents a major public health concern. In some endemic countries in the Mediterranean region, long-established control programs have achieved 80-100% prevention of newly affected births. In Iran, it is estimated that about 8,000 pregnancies are at risk each year. Fars province, located in the southeast region of Iran, is estimated to hold about 10% of Iranian $\beta$-thalassemia patients while only 5% of the total population. A program for the prevention of $\beta$-thalassemia in Iran, particularly in Fars province, was instigated a decade ago. At that time, estimates stated that there was a 7% rate of $\beta$-thalassemia carriage among the population of Fars province. This study aims to collect regional mapping data on the gene frequency of $\beta$-thalassemia in Fars province.  

Materials and Methods  

To evaluate the prevalence of $\beta$-thalassemia minor, all males in their final year of high school were selected as the sample group in the 13 regions in Fars province, Iran. Jahrom and Fasa, two regions with independent health care systems from Fars province, were not included in the study. The study was explained to the subjects and fortunately all agreed to participate in the study. Finally, 24,485 boys were examined.  

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After a complete blood count, boys with a mean corpuscular volume (MCV) of below 80 FL and red blood cell count (RBC) of above 6.1? 10^{12}/L were considered as the suspected group. HbA2 levels were measured for this group using Hb electrophoresis. Individuals with HbA2 levels higher than 3.5% were considered minor β–thalassemia. Those with HbA2 levels lower than 3.5% were treated for two months with oral iron (one ferrous sulfate tablet equivalent to 50 mg Fe^{2+}, tid). The tests were repeated after this period and a decision was reached using the same algorithm as above (individuals with HbA2 level of higher than 3.5% were considered minor β–thalassemia and others were considered iron deficiency anemia).

All patients with major β–thalassemia are registered by the regional health care centers. Using the information on registration sheets, these patients or their families were contacted. Data on sex, age and consanguinity of parents were obtained by face to face interview. Data on the total population of the area was obtained from the Budget and Program Organization of Iran, Fars branch, Shiraz and Statistical Center of Iran, Tehran.

The results were analyzed using EPI6.04 software.

**Results**

Mean Hb in the whole region was 14.91 g/dL with a standard deviation (SD) of 1.4 g/dL. Mean MCV in the whole region was 83.67 fl with a SD of 4.6 fl. Mean RBC count was 5.57? 10^{12}/L with a SD of 0.3? 10^{12}/L.

The frequency of minor β–thalassemia was 6.88% (95% CI=6.57%-7.2%) in the whole province. It ranged from 3.2% to 10.52% in different areas. In Shiraz, the capital city of the province, the prevalence was 7.05%.

There were a total of 2,193 major β–thalassemia patients in Fars province. These patients consisted of 1,263 (57.6%) boys and 930 (42.4%) girls. The frequency of major β–thalassemia was 7.2 in 10,000 (95% CI= 6.9-7.5 in 10,000) population in the whole region. It ranged from 1 in 10,000 in Abadeh to 11 in 10,000 in Shiraz.

The frequency of β–thalassemia gene was 3.64% in the whole province. It ranged from 1.64% to 5.6% in different regions. In Shiraz the gene frequency was 3.77%. The regional mapping of β–thalassemia gene frequency in Fars province is depicted in **Figure 1**.

Mean age of the patients was 10.1 years with a SD of 6.6 years. **Figure 2** depicts the age distribution of patients with β–thalassemia major in Fars province. There was a decrease in prevalence of major β–thalassemias in the under-10-year-old population. However, this decrease was minimal after adjustment for population age distribution.

Parents were relatives in 1,453 (66.25%) of the major β–thalassemia patients. There was no relation between parents in 740 (33.75%) of the patients. However, no control group was obtained to evaluate the effect of consanguinity.

**Discussion**

Thalassemia is a global problem, endemic all over the world. Its foci of origination and prevalence are
the Mediterranean,\textsuperscript{5,6} Asia,\textsuperscript{7-9} and Africa,\textsuperscript{10,11} spreading throughout Europe,\textsuperscript{12} the Americas,\textsuperscript{13,14} and Australia due to population migration. In the eastern Mediterranean region, the prevalence of heterozygous β–thalassemia varies from about 3.5 - 4.5\% in the Gaza Strip\textsuperscript{6} and Jordan\textsuperscript{15,16} to 5.5\% in Pakistan.\textsuperscript{17}

Among the eastern Mediterranean region, Iran is one of the major centers for the prevalence of β–thalassemia. It is estimated that there are three millions β–thalassemia carriers and 25,000 patients in Iran. Fars province, located in the southeast region of Iran, is the focus of β–thalassemia in this country. It is estimated to hold about 10\% of Iranian thalassemia patients while only 5\% of the total population.\textsuperscript{4}

Our study shows a 6.88\% prevalence of minor β–thalassemias in Fars province. This is not significantly different from the previous 6.95\% result of a study by Karimi, et al. some five years ago.\textsuperscript{4} Since the study group consisted of 17-18 year-old boys, it did not attempt to evaluate the effect of the program for the prevention of β–thalassemia started a decade ago and thus a reduction in the rate of minor β–thalassemia was not expected. Moreover, since the program attempts to control the problem by preventing marriage of heterozygous individuals, a reduction in the rate of minor β–thalassemia can not be expected at all.

It can be clearly understood from Figure 1 that the frequency of the β-thalassemia gene declines in northern regions of Fars province, except for the focus of Marvdasht located above the center of the province. In a previous study by Merat et al., mutations from distant regions were observed among β–thalassemia mutations of this region. Migration of chromosomes from distant places and genetic admixture in this province was suggested.\textsuperscript{18} The relation between the pattern of migration and this map remains a question needing further investigation.

Figure 2 depicts the decrease in prevalence of major β–thalassemias in the under-10-year-old population. However, this decrease diminishes after adjustment for population age distribution. The loss of decrease in under 10-year-old population after adjustment shows that the program for the prevention of β–thalassemia has had moderate success. A large part of the decrease in prevalence of major β–thalassemias is in the under-10-year-old population and is, in fact, the result of the birth control program, rather than the program for the prevention of β–thalassemia. Studying the reasons for the short falls of the program and setting up new strategies are recommended.

Conclusion

The prevalence of minor and major β–thalassemia declines in northern regions of Fars province. The relation between the pattern of migration and this map remains a question needing further investigation.

The program for the prevention of β–thalassemia, started a decade ago, has proved moderately successful. Studying the reasons for the short falls of the program and setting up new strategies are recommended.

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