Thalassemia major and consanguinity in Shiraz city, Iran

Ali Akbar ASADI-POOYA[1], Mehrnoosh DOROUDCHI[2]

[1] Department of Pediatrics, Shiraz Medical School, Shiraz/Fars,
[2] Department of Immunology, Shiraz Medical School, Shiraz/Fars, Islamic Republic of IRAN

Turk J Haematol 2004;21(3): 127-130

Received: *17.03.2004* ***Accepted:*** *18.05.2004*

ABSTRACT

Beta-thalassemia is among the most common genetic disorders in the world and in Iran, with widespread occurrence. A cross-sectional study on 648 beta-thalassemia patients in Shiraz, Iran was carried out to determine the demography of beta-thalassemia major in Shiraz city, Fars province, Iran and also the rate of consanguinity and the significance of pre-marriage counseling in decreasing familial marriages and consequently preventing this autosomal recessive genetic disease. All interviewed patients had thalassemia major and their age, sex, and the consanguinity between parents were recorded. 40.6% of beta-thalassemia patients were outcomes of first-cousin marriages. Comparison of the percentages of familial marriages (consanguinity) between parents of beta-thalassemia patients and a sample of normal population, revealed a statistically significant difference ($p < 0.00001$). A nonstatistically significant difference was observed between male (53.5%) and female (46.5%) thalassemia patients. Comparison of data with the situation in 22 years ago revealed a 16.4% decrease in familial marriages among thalassemic families, however, more education and awareness of young women and men about the increased risk of beta-thalassemia after familial marriage through pre-marriage counseling is still necessary.

Key Words: Beta-thalassemia, Consanguinity, Sex ratio.

ÖZET

İran, Şiraz şehrinde talasemi majör ve akrabalık

Beta-talasemi, dünyada ve İran'da en sık rastlanan genetik bozukluktur. İran Şiraz kentinde beta-talasemi majörün demografisini saptamak için 648 beta-talasemi hastasında kesitsel bir çalışma yapıldı. Bu sırada akrabalık oranı, aile içi evlilikleri azaltmak için evlilik öncesi danışma ve bunların otozomal resesif genetik hastalığı önlemeye etkisine bakıldı. Çalışmaya talasemi majörlü hastalar alındı ve onların yaşı, cinsiyeti ve aralarındaki akrabalıklar sorgulandı. Beta-talasemili hastaların %40.6'sı ilk kuzen evliliği sonucu idi. Beta-talasemili hastaların aile içi evlilikleri ile normal toplum karşılaştırıldığında istatistiksel olarak anlamlı bir fark görüldü

(p< 0.00001). Erkek ve kadın beta-talasemik hastalar arasında bu açıdan fark görülmedi. Aynı konuda 22 yıl önce elde edilen verilerin karşılaştırılmasında aile içi evliliklerde %16.4 azalma görüldü. Ancak, evlilik öncesi danışma yolu ile aile içi evliliklerde beta-talasemi riskinin artışı hakkında eğitim ve bilgilendirme halen gereklidir.

Anahtar Kelimeler: Beta-talassemi, Akrabalık.

INTRODUCTION

Beta-thalassemia is among the most common genetic disorders in Iran and in the world[1-3]. In Iran, the gene frequency of beta-thalassemia is high but varies considerably from area to area, having its highest rate of more than 10% around the Caspian sea and Persian Gulf [4,5]. In Fars province, in southern Iran, the gene frequency is also high and reaches 8-10%[5].

The disease is characterized by severe anemia resulting from reduction or loss of beta-globin chains or the imbalance between alpha and beta-globin chains[3]. Beta-globin gene is placed on the short arm of chromosome 11 adjacent to the embryonic (∈) gene, fetal γ (Gγ and Aγ) genes and adult delta gene[6]. Inheritance of two mutated alleles in beta locus (homozygous state) results in thalassemia major. The affected children suffer from severe anemia and need regular blood transfusion due to the destruction of red blood cell precursors in the bone marrow[7]. Thalassemia is considered to be a single-gene disease transmitted by a recessive mode of inheritance. The pattern of mutations of beta-globin gene in Fars province differs from those reported for the Mediterranean and other thalassemic regions in Iran[8]. This study way conducted to determine the demography of beta-thalassemia major in Shiraz city, Fars province, Iran. Also the rate of consanguinity in thalassemic families in comparison to normal population and the significance of pre-marriage counseling in decreasing familial marriages (consanguinity) and consequently preventing this autosomal recessive genetic disease was evaluated.

MATERIALS and METHODS

In total, 648 thalassemia major patients were included in this cross-sectional study. These patients were all of registered beta-thalassemia individuals in Shiraz city who were referred to the only Cooley's clinic in Shiraz located in the Dastegheib hospital, Shiraz, Iran in Spring 2003. Only those patients that their disease was diagnosed before two years of age and received blood transfusion every 3 to 4 weeks and desferrioxamine regularly in this unit, were interviewed. The required data including their age, sex, chelation therapy and the consanguinity between parents were collected by the authors by means of interview (patients and/or their parents) and reviewing their files after obtaining their (patients and/or their parents) permission.

Statistical analysis was performed by Chi-square and Z test using EPI info-6 software.

RESULTS

The total number of registered thalassemic patients in Shiraz city who were referred to Cooley's clinic for blood transfusion in Spring 2003 was 648 and the total number of registered thalassemia intermedia patients in the same duration was 110 individuals. All intermedia patients were excluded from this study. The mean age of patients was 11.8 ± 5 years. Of the 648 thalassemia major patients who were interviewed, 347 (53.5%) were male and 301 (46.5%) were female. A non-statistically significant difference was observed between number of male and female thalassemia patients (p= 0.07).

It was noticed that in approximately 49.5% of cases, the patients were outcomes of first-or second-cousin marriages. In 311 of the total 648 families of interviewed patients, parents were first or second cousin relatives and in 317 families parents had no relation to each other. In 255 of 311 (40.6%) families,

first-cousin marriage and in 56 of 311 (8.9%) families second-cousin marriage was observed. The total number of first-cousin and second-cousin marriages in the community (studied in 6004 families) was noted to be 22.4% and 8.6% of total marriages, respectively (Table 1). The comparison of consanguinity between parents in thalassemic families and general population in the same area revealed a highly significant difference ($p< 0.00001$).

The mean age at the start of chelation therapy (desferrioxamine) was 5.3 ± 3.4 among the patients. In total, for 104 out of 648 (16%) patients desferrioxamine therapy had been started after 10 years of age. Among females, 44 out of 301 (14.6%) individuals, therapy had been started after 10 years of age and among males, for 60 out of 347 (17.3%) individuals, therapy had been started after 10 years of age. The observed difference between males and females was not significant.

DISCUSSION

The present study provides information on 648 beta-thalassemia patients in Shiraz city in Spring 2003. In 40.6% of studied families, beta-thalassemic patients were outcome of first-cousin marriages. Comparing this with the previously reported 57% first-cousin marriages in affected families revealed 16.4% decrease in first-cousin marriage among high-risk families[9]. This significant decrease is the result of pre-marriage counseling and awareness of the general population about thalassemia major[10]. However, we still observed a highly significant association between beta-thalassemia and first-cousin marriage as compared to the whole community ($p< 0.00001$). In this regard, more education and awareness of young individuals about the increased risk of beta-thalassemia after familial marriages, population or premarital screening for heterozygote detection specially in this region in which the gene frequency is high, and finally pre-marriage counseling are all necessary for an effective prevention program.

A nonstatistically significant difference was observed between number of male and female thalassemia patients ($p= 0.07$). The number of affected males was more than affected females. The same excess of males over females was reported by Hashemi Nasab in 1979 among 140 beta-thalassemic patients in the same geographic area[9]. He suggested that this excess might be due to more concern of villagers about health of their male offspring, however, the studied population of the present report was an urban population with different economical and educational situations, which does not include villagers. In addition, as it was noted, the percentage of female subjects who started chelating therapy before 10 years of age was higher than male subjects (85.4% vs. 82.7%) which is indicative of people's concern about the health of their female offspring.

This sex-ratio difference in thalassemic patients (males more affected than females) is noteworthy and deserves further investigation considering thalassemia as a single-gene disease transmitted by a recessive mode of inheritance.

Table 1. The percentages of familial relation (consanguinity) between parents of beta-thalassemia patients compared to a sample of general population*

	First cousin (%)	Second cousin (%)	No relation (%)	Total
Patients families	255 (40.6)	56 (8.9)	317(50.5)	628
Normal families*	1344 (22.4)	519 (8.6)	4141 (69)	6004

* The percentages of familial relation between parents in 6004 families inhabiting Shiraz city (Saadat M et al unpublished data).

Acknowledgement

The authors would like to thank Dr. Mustafa Saadat from Department of Biology, Shiraz University, for his invaluable help and comments in preparing the manuscript. This work was financially supported by Shiraz University of Medical Sciences, Shiraz, Iran.

REFERENCES

1. Najmabadi H, Karimi-Nejad R, Sahebjam S, Pourfarzad F, Teimourian S, Sahebjam F, Amirizadeh N, Karimi-Nejad MH. The beta-thalassemia mutation spectrum in the Iranian population. Hemoglobin 2001;25:285-96.
2. Merat A, Haghshenas M, Mostafavi Pour Z, Plonczynski MW, Harrel AN, Coleman MB, Steinberg MH. Beta-thalassemia in Southwestern Iran. Hemoglobin 1993;17:427-37.
3. Thein SL. Beta-thalassemia. Bailliere's Clin Hematol 1998;11:91-126.
4. Merat A, Haghshenas M. The spectrum of beta-thalassemia mutations in Iran. Med J I R Iran 2000; 14:103-6.
5. Habibzadeh F, Yadollahie M, Merat A, Haghshenas M. Thalassemia in Iran; an overview. Arch Irn Med 1998;1:27-33.
6. Collins FS, Weissman SM. The molecular genetics of human hemoglobin. Prog Nucleic Acid Res Mol Biol 1984;31:315-465.
7. Colah R, Mohanty D. Beta-thalassemia: expression, molecular mechanisms and mutations in Indians. Indian J Pediatr 1998;65:815-23.
8. Mahboudi F, Zeinali S, Merat A, Delmaghani S, Mostafavipour K, Moghaddam Z, Haghshenas M. The molecular basis of beta-thalassemia mutations in Fars province, Iran. Irn J Med Sci 1996;21:99-104.
9. Hashemi Nasab A. Clinical and laboratory findings in the initial diagnosis of homozygous beta thalassemia in Fars province, Iran. Br J Haematol 1979;43:57-61.
10. Ghanei M, Adibi P, Movahedi M, Khami MA, Ghasemi RL, Azarm T, Zolghaderi B, Jamshidi HR, Sadri R. Pre-marriage prevention of thalassemia. Report of a 100.000 case experience in Isfahan. Public Health 1997;111:153-6.

Address for Correspondence:

Ali Akbar ASADI-POOYA, MD

Department of Pediatrics
Shiraz Medical School
Shiraz/Fars, Islamic Republic of IRAN