Reproductive behaviour of mothers of children with beta-thalassaemia major

F. Habibzadeh,[1] M. Yadollahie,[1] M. Roshanipoor[1] and M. Haghshenas[2]

السلوك الإنجابي لأمهات الأطفال المصابين بالثلاسيمية-بيتا الكبرى

فرخ حبيب زادة، محبوبة يد اللهي، مينارُوشَني بور، منصور حق شناس

الخلاصة: تعد الثلاسيمية من أكثر الأمراض الوراثية المنتقلة بالجينات الجسدية انتشاراً في العالم. وقد أجرى الباحثون دراسة مستعرضة ترتكز على استبيان للنظر في السلوك الإنجابي لدى 156 أمّاً من أمَّهات الأطفال المصابين بالثلاسيمية-بيتا الكبرى في ولاية فارس جنوب جمهورية إيران الإسلامية. وتبيَّنَ أنه بغضِّ النظر عن عدد الأطفال المصابين، فإن آباء وأمهات الأطفال المصابين بفقر دم كولي لديهم في المتوسط ثلاثة أطفال غير مصابين، وهو مماثل للمتوسط المقابل لدى سكان الولاية. كما اتضح أن لتقديم المشورة الوراثية دوراً هاماً في تخفيض عدد الأطفال المولودين، سواءً تم تقديم المشورة الوراثية قبل الزواج أو بعد ولادة أول طفل مصاب. وتشير نتائج البحث إلى حدوث التعويض الإنجابي في الأسر التي لديها طفل مصاب بفقر دم كولي في هذه الولاية.

ABSTRACT Thalassaemia is the most common monogenic autosomal hereditary disease worldwide. This questionnaire-based cross-sectional study looked at the reproductive behaviour of 156 mothers of children affected with beta-thalassaemia major (Cooley anaemia) in Fars province, southern Islamic Republic of Iran. Regardless of the number of affected children, the parents of children with Cooley anaemia had an average of 3 unaffected children, the same as the average for the provincial population. The findings indicate that reproductive compensation occurs in families with a child with Cooley anaemia in this province. Genetic counselling, either before marriage or after the birth of the first affected child, had a significant effect on lowering the number of children born.

Comportement en matière de procréation des mères d'enfants atteints de β-thalassémie majeure

RÉSUMÉ La thalassémie est la maladie héréditaire monogénique à transmission autosomique la plus fréquente dans le monde. La présente étude transversale reposant sur un questionnaire a évalué le comportement en matière de procréation de 156 mères d'enfants affectés par une β-thalassémie majeure (aussi appelée anémie de Cooley) dans la province de Fars (sud de la République islamique d'Iran). Sans tenir compte du nombre d'enfants affectés, les parents d'enfants atteints d'une anémie de Cooley avaient en moyenne trois enfants non touchés par la maladie, c'est-à-dire le même nombre que dans la population de la province. Les résultats indiquent qu'une compensation reproductrice se produit dans les familles ayant un enfant atteint de l'anémie de Cooley dans cette province. Les conseils génétiques, soit avant le mariage soit après la naissance du premier enfant affecté, ont eu un effet significatif sur la réduction du nombre d'enfants nés.

[1]Medical Education and Research Centre, National Iranian Oil Company Health Organization, Shiraz, Islamic Republic of Iran (Correspondence to F. Habibzadeh: farrokh.habibzadeh@gmail.com).
[2]Haematology Research Centre, Shiraz University of Medical Sciences, Shiraz, Islamic Republic of Iran.

Received: 04/12/07; accepted: 24/03/08

Introduction

Thalassaemia is an inherited blood disease that affects tens of thousands of people worldwide. It is the most common monogenic autosomal hereditary disease worldwide [1]. Hypothetically, this haemoglobinopathy serves a useful purpose in populations as there is evidence that it is protective against fatal falciparum malaria. Nowadays, however, with eradication of malaria from many countries, thalassaemia has become an important socioeconomic burden for these countries [2]. The cost of medical services provided to almost 25 000 patients with thalassaemia major in the Islamic Republic of Iran exceeds US$ 40 million annually. The distribution of the gene for thalassaemia, however, is not uniform, with the highest prevalence in the Mediterranean area, North and West Africa, the Middle East, the Indian subcontinent, southern Far East and south-eastern Asia: the so-called "thalassaemia belt" [1].

In view of the considerable problems facing the families of these children, it would be expected that giving birth to a child with thalassaemia would have an impact on the subsequent reproductive behaviour of a couple. Several studies have been conducted on this issue; some have indicated a reproductive compensation in families with a child with Cooley anaemia [3–5], while another concluded that there was no reproductive compensation [6]. Since this behaviour presumably depends to a great extent on the cultural backgrounds of the families, and in view of the existing controversy, we conducted this research to study the reproductive behaviour of mothers of children with beta-thalassaemia major in Fars province, southern Islamic Republic of Iran.

Methods

Fars province has almost 2500 patients with beta-thalassaemia major [2]. Many of these patients receive medical services in Shiraz, the Capital of Fars province. Thalassaemia patients receive a blood transfusion every 3 to 6 weeks.

In a questionnaire-based, cross-sectional study over 1 week in July 2005, the mothers of all patients who attended the Cooley anaemia centre of Dastgheib hospital, affiliated to Shiraz University of Medical Sciences, were interviewed either by a trained registered nurse or a general practitioner. Both interviewers were trained for the job at the Medical Education and Research Centre of the National Iranian Oil Company Health Organization. The objectives of the study were described to participants and their consent was taken before enrolment into the study. Each mother was asked whether she had had genetic counselling before marriage or after the birth of her first affected child; about the couple's desire to have more children and the age, sex and the health status of her children in order of birth.

Data were coded and analysed by *Epi-Info*, version 6, and *SPSS*, version 14.0 for Windows. Statistics were presented as mean and standard deviation (SD). The Mann–Whitney U-test was used to compare the mean number of children between 2 groups, and Kruskal–Wallis 1-way analysis of variance (ANOVA) used for comparisons among 3 or more groups. $P < 0.05$ was considered statistically significant.

Results

Over the study period of 1 week, 164 mothers of children with beta-thalassaemia major attended the anaemia centre; 156 consented to take part in the study and were interviewed. The data for all these participants were complete and analysed. The remaining 8 mothers refused to participate in this study for personal reasons.

These 156 mothers had a mean total number of children of 4.34 (SD 2.24) (Table 1). Each mother had a mean of 1.45 (SD 0.81) children with Cooley anaemia, dead or alive. This translates into a mean number of unaffected children of 2.93 (SD 2.04) (Figure 1).

Only 7 (4.5%) mothers had received genetic counselling before marriage (Table 2). Those who had had premarital genetic counselling had a significantly lower mean total number of children [2.14 (SD 1.07)] than those who had not [4.81 (SD 2.28)] ($P = 0.0017$; Mann–Whitney U-test). There were 36 mothers (23.1%) who had sought genetic counselling after they gave birth to their 1st child with thalassaemia. The mean number of children of mothers who had sought genetic counselling [3.39 (SD 1.68)] was also significantly lower than that of those who had not [(4.81 (SD 2.28)] ($P = 0.0013$; Mann–Whitney U-test) (Table 2).

Those women whose 1st or 2nd child had Cooley anaemia ($n = 82$)

Table 1 Effect of birth of a child with beta-thalassaemia major on the total number of children in each family

Parameter	No. of children with beta-thalassaemia major (dead or alive)			
	1	2	3	4
Number of families	107	35	10	2
Mean (SD) number of children[a]	3.69 (2.01)	5.86 (2.00)	5.20 (1.55)	7.50 (2.12)

[a]Means were significantly different (P < 0.001; Kruskal-Wallis 1-way ANOVA).
SD = standard deviation.

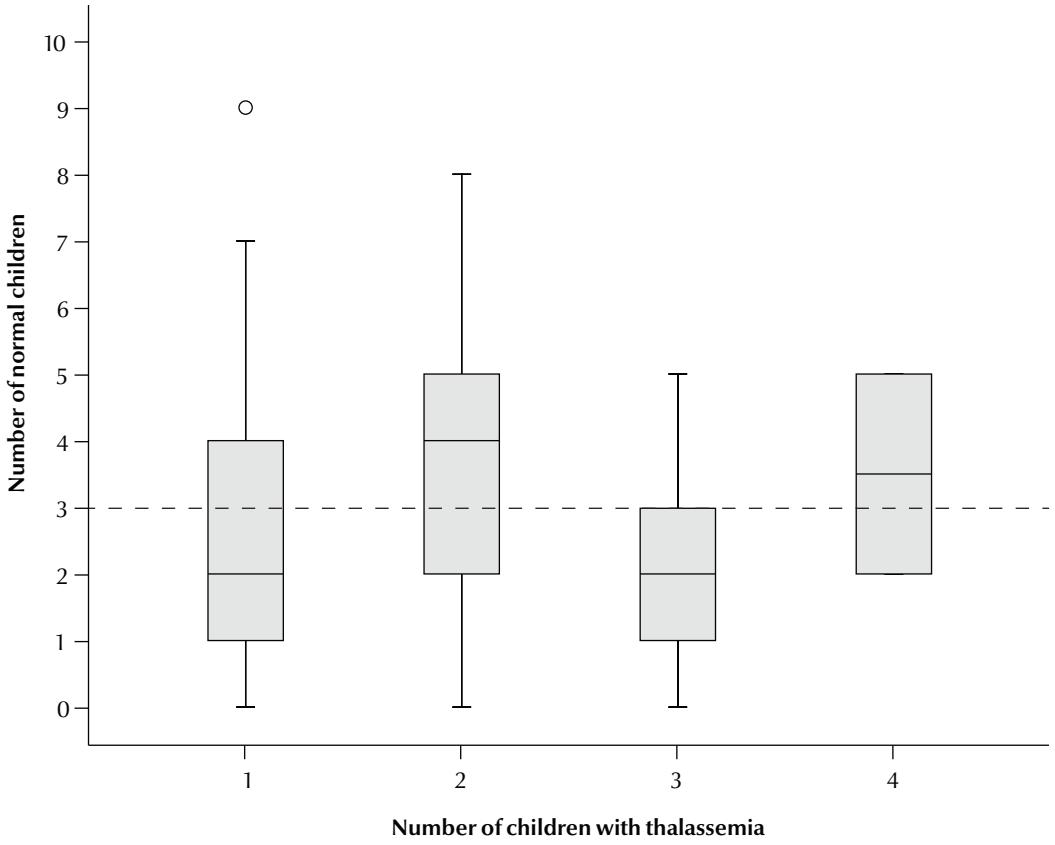

Figure 1 Minimum, 25th, 50th, 75th percentiles and maximum number of normal children in families with 1–4 children with beta-thalassaemia major (dead or alive). Dashed line indicates the average number of 3 children in families of Fars province (the small circle above the left box is an outlier, defined as values 1.5–3 times the interquartile range)

had a mean total number of 3.12 (SD 1.88) children; for those whose first affected child was either the 3rd or 4th child (n = 38), the value was 4.53 (SD 1.12); and for those whose first affected child was the 5th child or later (n = 36), the mean was 7.08 (SD 1.68) (P < 0.0001; Kruskal–Wallis 1-way ANOVA).

For women with at least 1 healthy live boy among their first 3 children (n = 93), the mean total number of children was 1.42 (SD 0.80), while for the remaining women (n = 63), it was 1.49 (SD 0.84) (P = 0.5855; Mann–Whitney U-test).

A total of 16 mothers (10.7%) wished to have more children. This was not correlated with their number of children, number of thalassaemic children, previous genetic counselling or with any other parameters studied.

Discussion

The mean family size of the population of Fars province is around 5, i.e. a couple with their 3 children [7]. We found that regardless of the number of affected children, parents of patients with Cooley anaemia had an average of 3 additional children so that these families had the same mean number of 3 unaffected children as families in the

Table 2 Effect of genetic counselling on the total number of children and number of affected children in each family

Parameter	Genetic counselling received			*P*-value
	Premarital	After birth of an affected child	None	
Number (%) of families	7 (4.5)	36[a] (23.1)	114 (73.1)	–
Mean (SD) number of children	2.14 (1.07)	3.39 (1.68)	4.81 (2.28)	0.0013
Mean (SD) number of children with beta-thalassaemia	1.00 (0.00)	1.34 (0.59)	1.51 (0.89)	0.150

[a]1 mother had counselling both before marriage and after giving birth to an affected child.
SD = standard deviation.

provincial population (Figure 1). Similar observations were made by Cowan and Kerr [8]. They reported that 67% of families with both their 1st and 2nd children affected by beta-thalassaemia major had additional children, whereas 37%–38% of those with only 1 of their 1st or 2nd child affected did so [8].

Genetic counselling, either before marriage or after the birth of the 1st affected child had a significant effect on lowering the number of children born in this study. Therefore, in countries where thalassaemia is prevalent, one of the most effective ways to control the birth of thalassaemia patients is to establish a good counselling system [9]. We observed that only 4.5% of the mothers had received premarital counselling, but that after the birth of their 1st affected child, many of them (23.1%), although not all, sought medical counselling. Facing the problems of children with Cooley anaemia seemed to have a braking effect on the number of children born so that those mothers who experienced these problems earlier (with their 1st or 2nd child affected) had significantly fewer children than others. It has been shown, for example in the United Kingdom, that there are appreciable differences between different ethnic groups in their acceptance of genetic counselling [10].

Many researchers believe that there is a sex preference in favour of male children in some developing countries [11,12]. This male preference might cause families of patients with Cooley anaemia to give birth to children until they have enough boys. In our study, we did not observe such a sex preference. The mean number of children in those families with at least 1 of their first 3 children being male was almost equal that of other families. The mother's wish to have more children was correlated with none of parameters studied.

To the best of our knowledge, no such study has been conducted previously in the Islamic Republic of Iran. The number of mothers we interviewed was also higher than the sample size of many other studies reported worldwide [3,4,8]. However, our study suffered from lack of a matched comparison group.

In conclusion, it was found that couples having a child with Cooley anaemia had a higher reproductive rate which suggests that there is reproductive compensation in families with Cooley anaemia in Fars province. Genetic counselling, both before and after marriage, has a substantial effect on this compensatory mechanism. The Islamic Republic of Iran has found a combination of carrier screening and genetic counselling to be the most appropriate approach to preventing the birth of children with homozygous beta-thalassaemia [9].

References

1. Lukens JN. The thalassemia and related disorders, quantitative disorders of hemoglobin synthesis. In: Lee GR et al., eds. *Wintrobe's clinical haematology*, 9th ed. Philadelphia, Lea and Febiger, 1993:1102–1145.
2. Habibzadeh F et al. Thalassemia in Iran: an overview. *Archives of Iranian Medicine*, 1998, 1(1):27–33.
3. Aguzzi S, Vullo C, Barrai I: Reproductive compensation in families segregating for Cooley's anemia in Ferrara. *Annals of Human Genetics*, 1978, 42(2):153–160.
4. Rustamov R, Tokarev IuN. [Reproductive compensation in the mothers of patients with homozygous beta-thalassemia]. *Genetika*, 1983, 19(9):1545–1550 [in Russian].
5. Gamberini MR et al. Reproductive behavior of families segregating for Cooley's anemia before and after the availability of prenatal diagnosis. *Journal of Medical Genetics*, 1991, 28(8):523–529.
6. Gamberini MR et al. Reproductive behavior of thalassemic couples segregating for Cooley anemia. *American Journal of Medical Genetics*, 1991, 38(1):103–106.
7. Yazdanbakhsh M, Jamshidi Z. *Fars statistical year book (2002–2003)*. Fars, Deputy of Statistics and Informatics, Fars Management and Planning Organization, 2003:61–92.
8. Cowan J, Kerr C. Reproductive patterns and thalassaemia major. *Journal of Biosocial Science*, 1986, 18(3):285–295.
9. Samavat A, Modell B. Iranian national thalassemia screening programme. *British Medical Journal*, 2004, 329:1134–1137.
10. Modell B, Ward RHT, Fairweather DVI. Effect of introducing antenatal diagnosis on reproductive behaviour of families at risk for thalassaemia major. *British Medical Journal*, 1980, 280:1347–1350.
11. Goodkind D. Do parents prefer sons in North Korea? *Studies in Family Planning*, 1999, 30(3):212–218.
12. Liu H, Gu B. Preference of rural population on the sex of expected children and their corresponding behaviors. *Chinese Journal of Population Science*, 1998, 10(3):199–209.