Hemoglobin, 2013; 37(2): 124–137

ISSN: 0363-0269 print/1532-432X online
DOI: 10.3109/03630269.2013.772062

informa
healthcare

ORIGINAL ARTICLE

SECULAR TRENDS IN THE NATIONAL AND PROVINCIAL BIRTHS OF NEW THALASSEMIA CASES IN IRAN FROM 2001 TO 2006

Mahmoud Hadipour Dehshal,[1] Alireza Ahmadvand,[2] Sakineh Yousefi Darestani,[1] Mohsen Manshadi,[1] and Hassan Abolghasemi[3]

[1]*Blood Transfusion Research Centre, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran*

[2]*Research Centre for Rational Use of Drugs, Tehran University of Medical Sciences, Tehran, Iran*

[3]*Shabid Beheshti University of Medical Sciences, Tehran, Iran*

□ *Thalassemia is one of the genetic diseases for which there are only a few successful prevention protocols. In this study, we aimed to analyze data for thalassemia newborns in a period of 6 years to find out the geographical distribution of cases, the "high-risk" provinces in Iran, the causes of thalassemia newborn cases, the coverage rate of the prevention programs and the limitations of the thalassemia registration system.*

To further our aim, an analytic cross-sectional study was designed at the Iranian Blood Transfusion Organization (IBTO), Tehran, Iran. A questionnaire was then prepared to gather data from each of the 30 provincial centers to find out the number and causes of thalassemia births. Furthermore, another questionnaire, to be completed by the physicians in charge, was aimed at gathering data from all 207 thalassemia care centers. We then performed a stratified analysis of the frequency of distributions; the associations among the existing variables were evaluated using the χ^2 *or Fisher's exact tests at a 5.0% significance level.*

According to the findings, from 2001–2006, a total of 2091 thalassemia patients were born. The main causes were: the at-risk couples not using prenatal diagnosis (PND), marriages before the commencement of Iranian prevention plans, unregistered marriages based on religious conventions, among foreign citizens and the existence of some test errors. The causes of birth for 284 (13.6%) of new cases were not documented. There was a statistically significant difference between the five high-risk provinces regarding the proportional causes of thalassemia newborns [Pearson $\chi^2 = 4.549$*; degree of freedom (df)* $= 8$*,* p *value* $= 0.0001$*].*

Although the plan succeeded in avoiding the annual birth of 826 new cases on average, there is continuing concern that more than 300 new cases were born every year during 2001–2006 and new

Received 16 May 2012; Accepted 19 October 2012.

Address correspondence to Dr. Mahmoud Hadipour Dehshal, Iranian Blood Transfusion Organization (IBTO) Research Centre, 9th Floor, IBTO Main Building, Hemmat Expressway, Tehran, Iran; Tel.: +982188601582; Fax: 982188601580; E-mail: mehregan_hadipour@yahoo.com

prevention strategies need to be put into practice. It is highly recommended that focus be put on factors persistently causing the birth of new cases, especially in high-risk areas in which the success rates are lower than 50.0%.

Keywords Thalassemia, Iranian Thalassaemia Prevention Programme, Prevention success rate, Iran, Middle East, Genetic diseases

INTRODUCTION

Progress in controlling communicable diseases increases the relative importance of non communicable diseases including genetic disorders (1). Thalassemia is one of the genetic diseases mostly prevalent from the Mediterranean region to East Asia ("Thalassemia Belt"). Reportedly, there are a few successful thalassemia prevention protocols (Supplement 1) (2,3).

The Iranian Thalassaemia Prevention Programme was formed in 1995; however, it was only in 1997 when it was officially implemented by the government through the primary healthcare network and the National Genetics Committee. The network includes many institutions such as medical universities, health departments and rural health houses (4). The acceptability and effectiveness of preventing thalassemia by carrier screening and genetic counseling in high-risk populations is well established (5). The Iranian Thalassaemia Prevention Programme was designed to create a general infrastructure for the prevention of genetic disorders. Screening was included as part of the existing mandatory premarital blood testing. Initially, complete blood count tests were done in men to avoid stigmatization of women. Then, at-risk couples were offered information about thalassemia and genetic counseling because abortion after prenatal diagnosis (PND) was not allowed in Iran at the time (6).

After the start of the program, abortion for the prevention of thalassemia became legal by a religious verdict (Fatva) and genetic counseling became a part of the prevention program (3,6,7). Therefore, PND was offered at limited centers throughout the country (8). It was not until 2004 that the success of the program started to be evaluated. In 2004, Samavat and Modell (4) reported a significant decrease in the number of new cases with thalassemia between the years 1998 and 2002. In addition, Abolghasemi *et al.* (9) mentioned that the number of newly diagnosed cases has decreased considerably after the start of the prevention program.

Nevertheless, none of the researchers were aware of how successful the program had been in each of the 30 provinces of Iran. In 2008, Khorasani *et al.* (10) evaluated the success of the program in Mazandaran (a northern province of Iran). According to their findings, a great deal of suffering and an unbearable financial burden upon patients and their families had been prevented. They also reported that the number of registered patients at the Bou-Ali Sina Hospital in Sari, the capital city of Mazandaran, had declined from

500 in 1993 to an average of 35 per year during 1995–2005 (10). Nikuei *et al.* (11) reported the rate of success of the program in Hormozgan (a southern province of Iran). They declared that premarital screening in extended families, followed by PND, was acceptable as the most effective strategy for controlling thalassemia in developing countries (11).

The Iranian Thalassaemia Prevention Programme could be considered as a pattern for some Islamic and a few non Islamic countries. Some Islamic countries have already started a sort of prevention program which is similar to the Iranian model; however, these programs cover a limited area in their respective countries and they are only comparable to the Iranian model from the planning aspect (Supplement 2) (12–16). Furthermore, a few countries in Eastern Asia screened α- and β-thalassemia (α- and β-thal) in a limited number of regions (Supplement 3) (17–20).

Considering the importance of the Iranian national screening and the experiences of PND in this country as a pattern for Islamic or developing countries, we should reflect over the program from different aspects. We aimed at analyzing the data for thalassemia newborns for 6 years in order to find out the geographical distribution of cases, investigate "high-risk" provinces (those with over 100 cases of thalassemia during these years), weigh the relative importance of the causes of thalassemia newborn cases, study the coverage rate of the Iranian National Thalassemia Prevention Programme, and shed light on the limitations of the thalassemia registration system in the country.

MATERIALS AND METHODS

Study Design and Variables

An analytic cross-sectional study was designed for the analysis of data on a number of thalassemia newborns, their national and provincial distribution, and the causes of birth including those concerning at-risk couples who did not use PND, those who got married before the commencement of the Iranian prevention plan, children born after unregistered marriages based on religious conventions (the couples who get married and postpone marriage registration), children born to foreign citizens, screening test errors, and PND test errors.

Setting

We collected our data over the course of 6 years (2001 to 2006) from the national Iranian Blood Transfusion Organization (IBTO), Tehran, Iran. Because of the establishment of hemovigilance committees at all provincial blood centers of IBTO, we were able to access and include reliable

information from all thalassemia patients registered in the national thalassemia registry network across the country. Provincial carrier rates and affected births were gathered from the Genetics Office of the Disease Management Centre based at Iran's Ministry of Health and Medical Education (GO-MOH), Tehran, Iran.

Data Sources/Measurements

A questionnaire was sent to every provincial center in order to find out both the number and cause of newborns in each of the 30 provinces. The questionnaires were also sent to 207 thalassemia care centers distributed throughout the country; these were to be completed by the physicians in charge.

For every participant, each of these variables was defined and added to the dataset; an identification number, the province of birth, the city of birth, and the cause of birth (at-risk couples who did not use PND, those who got married before the commencement of the Iranian prevention plan, children born after unregistered marriages based on religious conventions, children born to foreign citizens, and test errors: "1" for positive and "0" for any negative causes).

Bias

Because of the lack of an online registration system, a considerable number of patients were registered 4 or 5 years after birth. Those patients with delayed registration who comprised a sizable proportion were mainly diagnosed as carriers of β-thal intermedia (β-TI). Thus, to avoid collecting incomplete information, we ignored the data of new cases with thalassemia in the 4 years that led to the present study.

Statistical Methods

The statistical analysis of the data was performed using the Statistical Package for Social Sciences version 16.0 software (SPSS Inc., Chicago, IL, USA). For descriptive statistics, we performed an analysis of the frequency distributions considering strata such as the year and province of birth, and the reason for being a thalassemia newborn. Because of the qualitative nature of the variables, associations among them were evaluated mostly using the χ^2 or Fisher's exact tests at a 5.0% significance level ($p = 0.05$) as appropriate. The success rate of the prevention program was defined by this formula: [1 – (observed thalassemia new cases/estimated expectation of thalassemia new cases)] * 100.

RESULTS

Descriptive Data

Our findings showed that 2091 thalassemia patients were born from 21 March 2001 to 21 March 2006. The numbers of patients born in the years 2001, 2002, 2003, 2004, 2005 and 2006 were 350, 375, 363, 325, 378 and 300, respectively (Figure 1). A total number of 684 patients (32.7%) out of 2091 newborns were registered in Sistan & Baluchistan, a province located in southeast Iran. After the establishment of DNA laboratories in Zahedan, the capital city of Sistan & Baluchistan, the number of new cases was 176 (25.7% of all the newborns in the province).

We defined a province as "high-risk" if more than 100 patients were born during the years of the study in that specific province; based on this definition, there were five provinces at risk including Sistan & Baluchistan, Hormozgan, Khuzestan, Fars, and Kerman, mainly located in south and southeast Iran. The total number of patients born in these five provinces was 1350 (64.5% of all cases). The geographical distribution of new cases throughout Iran from 2001 to 2006 is shown in Figure 2.

The causes of birth for 284 (13.6%) of the new cases were not documented at registration centers. For the remaining 1807 cases, the chief causes were as follows: at-risk couples who did not use PND, those who got married before the commencement of the Iranian prevention plan, children born after unregistered marriages based on religious conventions, and test errors

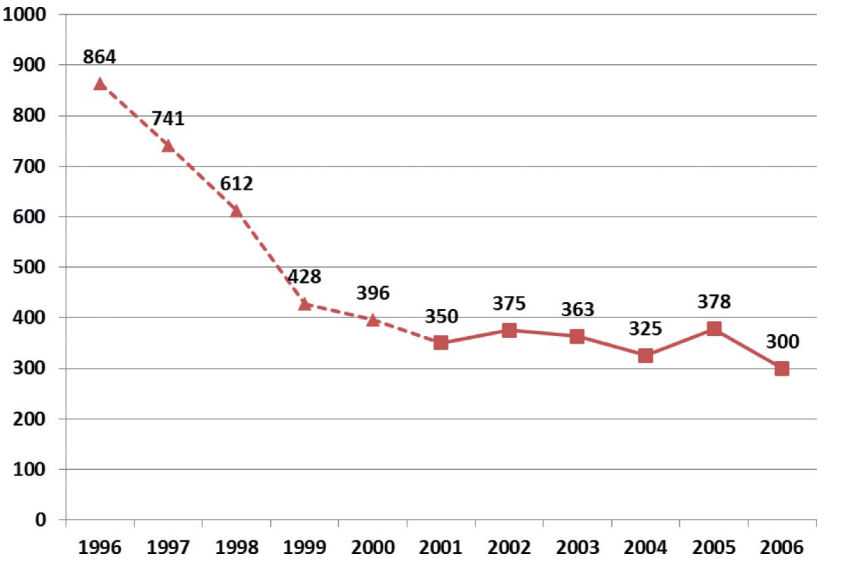

FIGURE 1 Number of new thalassemia cases born between 1996 and 2006 in Iran.

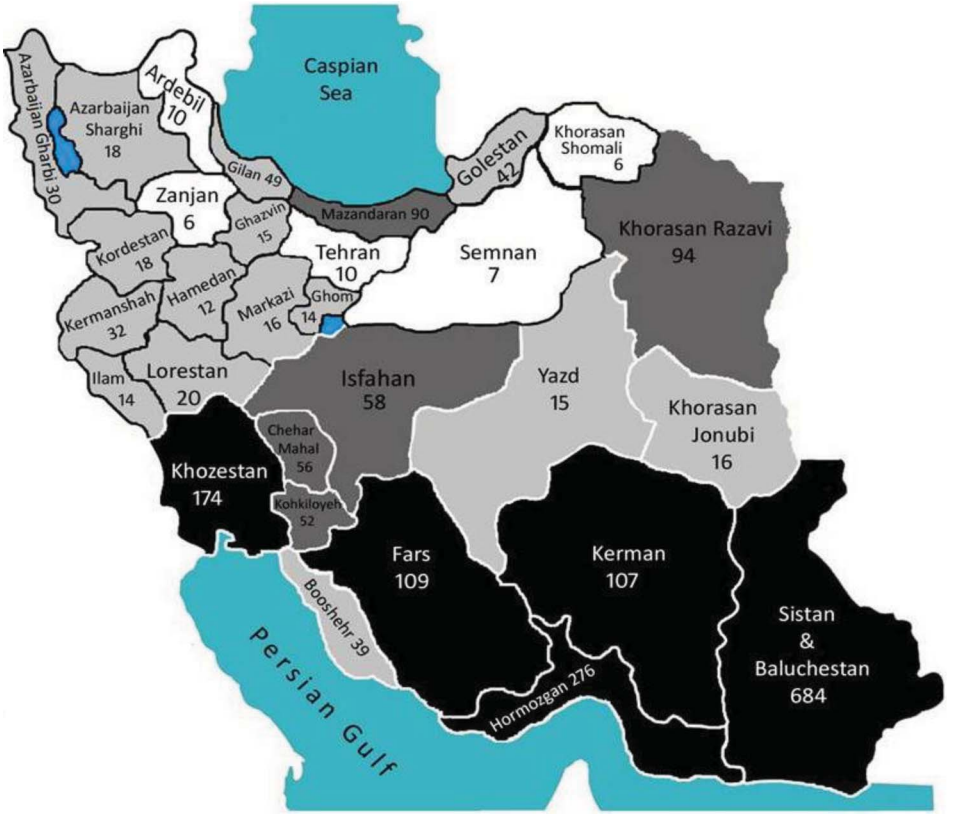

FIGURE 2 Geographical distribution of new thalassemia cases in Iran by province (2001-2006).

that are shown in table 1. The patients born due to not pursuing PND or a test error were covered by the Iranian Thalassaemia Prevention Programme and the ones born due to the three remaining reasons were uncovered by the program. Table 2 shows the percentages of program coverage per year.

Analysis

There was a statistically significant difference between the five at-risk provinces, regarding the proportional causes of thalassemia newborns [Pearson $\chi^2 = 4.549$; degree of freedom (df) $= 8$, p value $= 0.0001$]. There was also a statistically significant difference in the number of new cases covered or uncovered by the plan in each year between the years 2001 and 2006 (Pearson $\chi^2 = 18.573$; df $= 10$, p value $= 0.046$).

The observed number of new thalassemia cases from the years 1996 to 2005 was compared with the figures of the affected births provided by

TABLE 1 Number of New Thalassemia Cases in Iran According to Different Causes of Birth (2001–2006)

Year	2001	2002	2003	2004	2005	2006	Total
Expected β-TM births	809	816	852	840	897	912	5,126
Observed β-TM births	350	375	363	325	378	300	2,091
At-risk, not using PND	73	89	93	100	109	77	541
At-risk, not using PND (%)	9.02	10.91	10.92	11.90	12.15	8.44	10.55
Married before program	141	134	127	92	98	66	658
Married before program (%)	17.43	16.42	14.91	10.95	10.93	7.24	12.84
Unregistered marriage	70	80	70	77	109	102	508
Unregistered marriage (%)	8.65	9.80	8.22	9.17	12.15	11.18	9.91
Foreign citizens	2	12	13	7	7	13	54
Foreign citizens (%)	0.25	1.47	1.53	0.83	0.87	1.43	1.05
Screening test errors	10	14	10	16	14	14	78
Screening test errors (%)	1.24	1.72	1.17	1.90	1.56	1.54	1.52
PND test errors	0	1[a]	0	2[b]	0	1	4
PND test errors (%)	0	0.12	0	0.24	0	0.11	0.08
Unknown	54	46	50	33	41	28	252
Unknown (%)	6.67	5.64	5.87	3.93	4.57	3.08	4.92
Total (%)	43.3	46.1	42.6	38.9	42.1	33.0	40.9

[a] Delayed referral for abortion.
[b] One test error due to *in vitro* fertilization (IVF); one test error in PND.

TABLE 2 Number and Percentage of Newborns With β-Thalassemia Covered by the Iranian National Thalassemia Prevention Programme (2001–2006)

Year	Uncovered by the Program (%)	Covered by the Program (%)	Unknown Reasons (%)	Total Number of Patients (%)
2001	208 (59.4)	83 (23.7)	59 (16.9)	350 (100.0)
2002	218 (58.1)	104 (27.7)	53 (14.1)	375 (100.0)
2003	205 (56.5)	103 (34.8)	55 (15.2)	363 (100.0)
2004	169 (52.0)	113 (34.8)	43 (13.2)	325 (100.0)
2005	211 (55.8)	123 (22.5)	44 (11.6)	378 (100.0)
2006	178 (59.3)	92 (30.7)	30 (10.0)	300 (100.0)
Total	1189 (59.9)	618 (29.6)	284 (13.6)	2091 (100.0)

GO-MOH and those of theoretically expected major thalassemia births, estimated based on the report of Samavat and Modell (4). If we had considered the latter as our baseline, the estimated births avoided from 1996 to 2005 would have been 253, 368, 503, 679, 633, 695, 680, 738, 760, 782, and 878, respectively. However, supposing the former as the baseline, the estimated births avoided would have been 324, 438, 574, 750, 699, 762, 747, 809, 829, 856, and 954, respectively (Table 3).

The data of the provincial affected births provided by GO-MOH show the average success rate of just over 70.0% in Iran from 2001 to 2006. But the rates were less than 50.0% in eight provinces (Hormozgan, Sistan & Baluchistan, Charmahal Bakhtiari, Yazd, Khorasan, Hamedan, Azerbaijan

TABLE 3 Observed *versus* Expected Births of β-Thalassemia Major Cases in Iran From 1996–2006

Year	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Total births	1,187,903	1,179,260	1,185,639	1,177,557	1,095,165	1,112,193	1,122,104	1,171,573	1,154,368	1,233,873	1,253,506
Observed β-TM births	864	741	612	428	396	350	375	363	325	378	300
β-TM/1,000	0.73	0.63	0.52	0.36	0.36	0.31	0.33	0.31	0.28	0.31	0.24
Expected β-TM births[a]	864	958	962	956	797	809	816	852	840	897	912
Actual births as % of expected	100.0	86.4	71.0	50.0	49.7	43.3	45.9	42.6	38.7	42.1	32.9
Estimated births avoided	0	117	250	428	401	459	441	489	515	519	612
Expected β-TM births[b]	1,117	1,109	1,115	1,107	1,029	1,045	1,055	1,101	1,085	1,160	1,178
Actual births as % of expected	77.4	66.8	54.9	38.7	38.5	33.5	35.5	33.0	30.0	32.6	25.5
Estimated births avoided	253	368	503	679	633	695	680	738	760	782	878
Expected β-TM births[c]	1188	1179	1186	1178	1095	1112	1122	1172	1154	1234	1254
Actual births as % of expected	72.7	62.8	51.6	36.3	36.3	31.5	33.4	31.0	28.0	30.6	23.9
Estimated births avoided	324	438	574	750	699	762	747	809	829	856	954

[a] If expected, affected births = 0.73/1,000.
[b] If expected, affected births = 0.94/1,000 (4).
[c] If expected, affected births =1.0/1,000 (reported by the Genetics Office of the Disease Management Centre based in Iran's Ministry of Health and Medical Education).

Gharbi and Kohgiluyeh Boyer Ahmad). In spite of the sizeable number of new cases with thalassemia in Fars, Mazandaran, Khuzestan, and Kerman, the success rate of the prevention program in those provinces was above 80.0% (Table 4).

TABLE 4 Provincial Distribution of Success Rates in the Iranian Thalassaemia Prevention Programme (2001–2006)

Provinces	β Carriers (%)[a]	Affected Births/ 1,000 (%)[a]	Average Births/ Year[b]	Expected Average Affected Births/ Year	Observed Average β-TM Births/ Year	Estimated Expected Births (%)	Success Rate (%)
Tehran	1.9	0.2	176,786	35	2	4.71	95.29
Zanjan	4.9	0.8	16,112	13	1	7.76	92.24
Kurdistan	5.9	1.5	24,009	36	3	8.33	97.67
Kerman	9.5	3.1	51,459	160	18	11.18	88.82
Khuzestan	7.4	2.3	87,283	201	29	14.45	85.55
Mazandaran	8.0	2.2	39,409	87	15	17.30	82.70
Fars	6.7	1.5	69,507	104	18	17.42	82.58
Ilam	5.9	1.4	9,151	13	2	18.21	81.79
Gilan	5.6	1.4	28,823	40	8	20.24	79.76
Isfahan	4.0	0.7	62,836	44	10	21.98	78.02
Semnan	3.6	0.6	7,788	5	1	24.97	75.03
Azerbaijan Sharghi	1.7	0.2	57,687	12	3	26.00	74.00
Lorestan	2.6	0.4	30,687	12	3	26.92	73.08
Bushehr	5.7	1.4	16,210	23	7	28.64	7136
Iran	**4.0**	**1.0**	**1,175,297**	**1175**	**348**	**29.62**	**70.38**
Kermanshah	3.3	0.5	32,767	16	5	32.55	67.45
Golestan	3.9	0.6	31,618	19	7	36.90	63.10
Ardabil	2.5	0.2	21,141	4	2	39.42	60.58
Ghom	2.6	0.3	16,963	5	2	45.85	54.14
Markazi	2.5	0.3	18,362	6	3	48.41	51.59
Qazvin	2.7	0.3	17,104	5	3	48.72	51.28
			Success Rate Below 50.0%				
Hormozgan	9.0	3.0	28,862	87	46	53.13	46.87
Sistan & Baluchistan	8.5	2.7	69,938	189	114	60.37	39.63
Charmahal Bakhtiari	4.4	0.9	16,465	15	9	62.98	37.02
Yazd	1.5	0.2	17,394	3	3	71.86	28.14
Khorasan	1.7	0.2	13,403	27	19	72.12	27.88
Hamedan	1.6	0.1	26,754	3	2	75.76	25.24
Azerbaijan Gharbi	1.0	0.1	52,880	5	5	94.55	5.45
Kohgiluyeh Boyer Ahmad	2.3	0.4	13,001	5	9	166.66	66.66[c]

DISCUSSION

There have been some controversial views on the rate of the success of the Iranian Thalassaemia Prevention Programme. Although this program has been successful in decreasing the number of thalassemia newborns to a steady and quite stable figure, there is a continuing concern that more than 300 new cases were born every year from 2001 to 2006. We tried to investigate the new birth causes and their geographical distribution for the first time so that the information would assist decision-makers to develop new strategies and adjust the plan to the social aspects of each high-risk province.

Samavat and Modell (4) hold the belief that the program has been successful from economic aspects and in terms of decreasing new cases. Abolghasemi *et al.* (9) evaluated the program at two different periods. According to them, in the first period, the program had not fulfilled its goals because of the lack of access to PND; however, after legitimizing PND based on a religious verdict (Fatva) and establishing the DNA laboratories network in 1998, the plan sped up to achieve the determined targets. In addition, they suggested that a few new strategies be added to the program, especially those regarding unregistered marriages based on religious conventions in Sistan & Baluchistan and parents who got married before commencement of the program (9). The same positive opinion about the program can be found in the research conducted by Ghanei *et al.* (21), who evaluated the program in Isfahan Province for 3 years (from January 1993 to January 1996). Although they reported no new cases in the province during these years, our findings showed an average of 9.66 new cases per year in the province between the years 2001 and 2006. In addition, Kosaryan *et al.* (22) reported great success from 1996 to 2005 in Mazandaran Province, Iran. According to them, the program raised awareness, and changed attitude and practice in high-risk couples (22).

On the other hand, Ghotbi *et al.* (23) insisted on the necessity of revision in the program in order to improve its efficacy. Our evaluation of the Iranian Thalassaemia Prevention Programme shows that though the number of patients born annually decreased from 864 registered in 1996 (the year in which the program started) to an average of 348.5 per year (2001–2006). The number of new cases born in aforementioned years did not change considerably. There seems to be a "high-risk belt" extending from southeast to southwest Iran; thus, the reason for such a stable "endemic-like" distribution needs more detailed assessment. Nonetheless, with reliance on the affected births data, three provinces located in the high-risk belt could be considered as the successful provinces in meeting the prevention program targets.

Therefore, new strategies should be taken into account by decision-makers. To expand the coverage of the program, especially in Sistan & Baluchistan, where the highest number of new cases was reported, social

habits and conventions in these regions should be considered; this is highly recommended for Sistan & Baluchistan, which has large differences with major parts of the country not only in terms of its dominating religion, but also in its common lifestyle such as relations among tribe members, marriage bonds, and even in having residents who get across the border. Reportedly, even the attitude of women towards marriage with relatives in Sistan & Baluchistan is obviously different from that of women in other parts of the country (24,25). While Sistan & Baluchistan was replete with the new cases born after unregistered marriages (83.0% of all newborn cases), 41.0% of reported test errors were found in its adjacent high-risk province, Hormozgan. The discrepancy in proportional effects of the five chief causes of thalassemia birth in high-risk provinces can prove the necessity of providing a more flexible plan, according to which local committees are allowed to adjust the program to social and economic conditions in their provinces.

Regarding the sizeable number of new cases having been born under the coverage of the program (for test errors or not using PND), new strategies need to be put into place such as using the power of an audit and feedback system, which continuously evaluate the program in every province (an internal strategy) and/or recruiting the skills of independent investigators and researchers and enabling them to help multidisciplinary informed decision-making. Nevertheless, a notable decrease in the percentage of newborns born to parents not having used PND in 2006 (the last year of our study) could be a hopeful alarm, which shows that effectiveness of the DNA laboratories network is going to be enhanced after 7 years of its establishment (Table 1). But, to be confident about its effectiveness, we should analyze the newer data after 2006.

Furthermore, we found out that the number of new cases born to parents married before the commencement of the program had decreased substantially between 2001 and 2006; thus, there was a fading trend in the effectiveness of this cause of thalassemia births (Figure 2). Though the previous researchers were advised to focus on parents who got married before the commencement of the program, it is highly recommended to focus on the other causes especially "children born after unregistered marriages based on religious conventions" and "not using PND" (9).

Consulting knowledgeable sociologists and epidemiologists involved in all aspects of high-risk areas can be a vital step to achieve a local strategy, especially for a province such as Sistan & Baluchistan. Increasing the access of couples to PND is the highly prioritized duty of the Iranian public health care system.

The revision of the practical process of the thalassemia prevention program and the evaluation of couples' awareness of thalassemia prevention in those provinces where the success rate was calculated to be lower than 50.0%, are highly recommended. It is within the scope of the duties of the Iranian

healthcare managers to review the efficacy of the prevention program in provinces with low success rates, especially Kohgiluyeh Boyer Ahmad.

Limitations

Our study is based on the data gathered routinely by the Iranian National Thalassaemia Registration System throughout Iran. Thus, a few limitations in this system including the delay in registration of patients, incomplete data, and the lack of documentation for newborn causes, may affect the results of the study. These limitations are highly recommended to be addressed by both researchers and health care decision makers.

Due to delay in the registration of patients, the information for the years 2007 and 2008 was not considered reliable; data for these years can be included in future and upcoming studies. Regarding incomplete data and the lack of documentation, we only analyzed those records with known causes for newborn cases. We are eagerly following the issue and hopeful to reveal the analyses of new cases born after 2006.

We were able to find three cases born due to PND test error and one case born due to in *vitro* fertilization (IVF) in our study during 6 years; however, considering the fact that Iranian law is somehow strict about medical errors (26), it may be a concern for medical practitioners to report precise PND error data. Furthermore, an interdisciplinary cooperation is recommended to avoid thalassemia born due to IVF.

CONCLUSIONS

The Iranian Thalassaemia Prevention Programme seems to have reached its goal in the majority of provinces; nevertheless, the success rates of the program in a few provinces are not acceptable. The analysis highlights the case of eight provinces for decision makers and makes them aware that in six out of eight provinces the number of newborns was not so high to label them as high-risk. Therefore, re-evaluating the process of prevention programs in those eight provinces including Sistan & Baluchistan, Hormozgan and six others, seems to be prioritized. As Ghotbi *et al.* (23) suggested, the program needs further follow-up, especially in high-risk areas. The program should be adjusted to social and religious beliefs of particular areas like Sistan & Baluchistan. To achieve its target, the program should be more flexible and allow specialists, health sociologists and epidemiologists to get involved in the program's decision-making. In order to increase the access to PND, insurance coverage on PND should be expanded and the transport and accommodation fee for at-risk couples should be paid (9). Though the target needs to be met in the long-term, it is within the scope of duties of the government and national health decision-makers to improve both the quality and quantity of

DNA laboratories throughout the country. The analysis of newborns with thalassemia after 2006 can shed more light on the effectiveness of the genetic laboratories network in thalassemia prevention. If the pace of enhancement in the network efficacy keeps up with the results found in 2006, the current DNA laboratories network can be trusted as a system for couples covered by the program to access PND, and accordingly have thalassemia-free children. If a new strategy is incorporated into the program, a continuous and powerful audit is exercised, and a liberal decision-making is exerted to authorize local committees to adjust the program to their pertinent regions, the Iranian Thalassaemia Prevention Programme will be considered as an orienting model, not only for Middle Eastern countries, but also for all developing countries located on the "Thalassemia Belt."

ACKNOWLEDGMENTS

We would like to express our deepest gratitude to Mr. Mehdi Tabrizi (IBTO, Tehran, Iran) and Dr. Jasmine Milani (National Language Institute, Tehran, Iran) for all their assistance in drafting the present article. In addition, we would like to thank all managers of provincial blood transfusion centers in Iran for helping us gather the new cases and relevant information, and Dr. Kourosh Etemad and Dr. Ashraf Samavat (Genetics Office, Ministry of Health and Medical Education, Tehran, Iran) for furnishing us with carrier rates in Iran. Our thanks also go to Mrs. Maryam Mollaie (IBTO), Mrs. Bahareh Ahmadinezhad (IBTO) and Mr. Mohammad Javad Mohammadkhani (Shahid Beheshti University of Medical Sciences, Tehran, Iran) for their help.

Declaration of Interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

REFERENCES

1. Alwan A, Modell B. Recommendations for introducing genetics services into developing countries. Nat Rev Genet. 2003;4(1):61–68.
2. Bozkurt G. Results from the north Cyprus thalassemia prevention program. Hemoglobin. 2007;31(2):257–264.
3. Amato A, Grisanti P, Lerone M, *et al.* 35 Years of thalassemia screening program in Latium (Italy): outcome analysis and prevention prospects. Proceedings of the 12th International Conference on Thalassemia and Other Haemoglobinopathies held at Antalya, Turkey, May 11–14 2001.
4. Samavat A, Modell B. Iranian national thalassemia screening programme. Br Med J. 2004;329 (7475):1134–1137.
5. Alwan AA, Modell B. Community control of genetic and congenital disorders, Cairo: World Health Organization Regional Office for the Eastern Mediterranean, EMRO Technical Publications Series 24, 1997.

6. Report of a World Health Organization meeting on ethical issues in medical genetics. Proposed international guidelines on ethical issues in medical genetics and genetics services http://www.who.int/genomics/publications/en/ethicalguidelines1998.pdf (accessed February 19 2013).
7. Strauss BS. Genetic counseling for thalassemia in the Islamic Republic of Iran. Perspect Biol Med. 2009;52(3):364–376.
8. Najmabadi H, Ghamari A, Sahebjam F, *et al.* Fourteen-year experience of prenatal diagnosis of thalassemia in Iran. Community Genet. 2006;9(2):93–97.
9. Abolghasemi H, Amid A, Zeinali S, *et al.* Thalassemia in Iran: epidemiology, prevention, and management. J Pediatr Hematol Oncol. 2007;29(4):233–238.
10. Khorasani G, Kosaryan M, Vahidshahi K, Shakeri S, Nasehi MM. Results of the national program for prevention of β-thalassemia major in the Iranian Province of Mazandaran. Hemoglobin. 2008;32(3):263–271.
11. Nikuei P, Hadavi V, Rajaei M, Saberi M, Hajizade F, Najmabadi H. Prenatal diagnosis for β-thalassemia major in the Iranian province of Hormozgan. Hemoglobin. 2009;32(6):539–545.
12. Baig SM, Azhar A, Hassan H, *et al.* Prenatal diagnosis of β-thalassemia in Southern Punjab, Pakistan. Prenatal Diagn. 2006;26(10):903–905.
13. Alhamdan NA, Almazrou YY, Alswaidi FM, Choudhry AJ. Premarital screening for thalassemia and sickle cell disease in Saudi Arabia. Genet Med. 2007;9(6):372–377.
14. Abi Saad M, Aoun S, Maatouk P, *et al.* The thalassemia prevention program at the Chronic Care Center in Lebanon: a success story. Proceedings of the 12th International Conference on Thalassemia and Other Haemoglobinopathies held at Antalya, Turkey, May 11–14 2001.
15. Keskin A, Türk T, Polat A, Koyuncu H, Saracoglu B. Premarital screening of β-thalassemia trait in the province of Denizli, Turkey. Acta Haematol. 2000;104(1):31–33.
16. Altay Ç, Yilgör E, Beksac S, Gürgey A. Premarital screening of hemoglobinopathies: a pilot study in Turkey. Hum Hered. 1996;46(2):112–114.
17. Zhou YQ, Mo QH, Lu JH, *et al.* Large-scale population and prenatal diagnosis for α and β thalassemia in Zhuhai City of Guangdong Province. Zhonghua Yi Xue Yi Chuan Xue Za Zhi. 2008;25(3):256–261.
18. Kor-Anantakul O, Suwanrath CT, Leetanaporn R, Suntharasaj T, Liabsuetrakul T Rattanaprueksachart R. Prenatal diagnosis of thalassemia in Songklanagarind Hospital in southern Thailand. Southeast Asian J Trop Med Public Health. 1998;29(4):795–800.
19. Ratanasiri T, Charoenthong C, Komwilaisak R, *et al.* Prenatal prevention for severe thalassemia disease at Srinagarind Hospital. J Med Assoc Thailand. 2006;89(Suppl 4):S87–S93.
20. Ko TM, Xu X. Molecular study and prenatal diagnosis of α- and β-thalassemias in Chinese. J Formosal Med Assoc. 1998;97(1):5–15.
21. Ghanei M, Abidi P, Movahedi M, *et al.* Pre-marriage prevention of thalassemia: report of a 100000 case experience in Isfahan. Public Health. 1997;111(3):153–156.
22. Kosaryan M, Vahidshahi K, Siami R, Karimi H, Ehteshami S. Knowledge, attitude, and practice of reproductive behavior in Iranian minor thalassemia couples. Saudi Med J. 2009;30(6):835–839.
23. Ghotbi N, Tsukatani T. Evaluation of the National Health Policy of Thalassemia Screening in the Islamic Republic of Iran. East Mediterr Health J. 2005;11(3):308–318.
24. Abbasi-Shavazi MJ, McDonald M, Chavoshi MH. Changes in family, fertility behavior and attitudes in Iran; Working Paper in Demography and Sociology Program; Research School of Social Sciences; The Australian National University; No. 88; 2003.
25. Parvin P. Poverty alleviation in Sistan & Baluchestan: the case of Shirabad; Allameh Tabatabaii University. Published by the United Nations Development Program in the Islamic Republic of Iran; 2000.
26. Eshghi P, Cheraghali M. Legal, social, and economic consequences of transfusion-transmitted infections in Iran and in the world. Scientific J Iranian Blood Transf Organ. 2009;6(4):301–311.