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ORIGINAL ARTICLE

Evaluation of the National Prevention Program in Iran, 2007–2009: the Accomplishments and Challenges with Reflections on the Path Ahead

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Abstract

β-Thalassemia major (β-TM) is an inherited disease and efforts have been made in several countries to reduce the number of affected births. In the present study, we aimed to evaluate the Iranian thalassemia prevention program, considered to be an important program in the region. The time period of the present study ranges from 2007–2009, during which new thalassemic births and the relevant causes were evaluated throughout the country. A cross-sectional analytical study was conducted at the Iranian Blood Transfusion Organization (IBTO), Tehran, Iran. A questionnaire was forwarded to all blood centers of the IBTO so as to obtain information about the new cases of thalassemia and the causes of these thalassemic births. Provincial thalassemia societies also received the questionnaires so that screening and prenatal diagnosis (PND) errors would be recorded. The results showed that 755 new thalassemia cases were born during 2007–2009 with the average fall in affected thalassemia births of 80.82%. The main cause of the new births was attributed to unregistered ''timeless religious marriages'' based on the conventions of the Sunni community which accounted for 43.17% of all new cases mainly having occurred in Sistan & Baluchestan Province. Not using PND was evaluated to be another main cause. Although the prevention program has led to a great reduction in thalassemic births, new measures are required, including research on how to make the program compatible with social and economic conventions and norms of Sistan & Baluchestan Province. The province of Kohgiluyeh Boyer Ahmad also needs to be revisited in terms of the program efficacy.

Keywords

Causes of new thalassemia cases, fall in affected birth rates, Iranian Thalassaemia Prevention Programme, prenatal diagnosis, prevention of thalassemia, thalassemia

History

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Introduction

The success in controlling communicable diseases has also prompted health activists to think of the importance of prevention of non communicable diseases (1) such as thalassemia that stretches from North West Africa and the Mediterranean region to Southeast Asia known as the ''thalassemia belt'' (2). The Cypriot program gained momentum from 1979 and showed a large fall in thalassemic births (3). Greece started their prevention program in 1975 and after 35 years the reports indicate significant decrease in thalassemic births (4).

Thalassemia prevention in Iran was initiated in 1995, although it was not until 1997 when mandatory premarital screening was implemented. The national prevention network of Iran stretching from country-dispersed genetic committees to rural health houses has linked medical universities to the Center for Non-communicable Diseases of the Iran Ministry of Health (5).

To control new thalassemic births, appropriate strategies have been adopted by the program in which carrier couple screening and genetic counseling to at-risk couples are practiced (6). The Iran prevention program was initially based on screening the male partner, to avoid the stigmatization of women that could occur in the conservative society of Iran. If the male partner was diagnosed as a thalassemia carrier then the female partner was tested (5). In the initial years of the program, when there were obstacles for prenatal diagnosis (PND) to be implemented, at-risk couples received comprehensive information about thalassemia and expert genetic counseling (7).

However, the issuance of a religious fatwa (verdict) (8) in 1998 approved abortion in the beginning months of pregnancy when the fetus was found to be affected with thalassemia (7,9) and made PND accessible to at-risk couples. The couples

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Step 1	Step 2	Step 3	Step 4
1. A couple decides to marry			
2. The couple decides to register their intent to marry at the notary office			
3. The couple undergoes compulsory thalassemia screening			
4. The male candidate is the first to undergo screening[a]	MCH >27.0 pg or MCV <80.0 fL	The couple are officially allowed to get married	
5. MCH >27.0 pg or MCV <80.0 fL			If indices are normal and Hb A_2 is <3.5%
6. The female undergoes CBC testing	MCH >27.0 pg or MCV <80.0 fL		
7. MCH >27.0 pg or MCV <80.0 fL			
8. Hb A_2 level in both male and female is evaluated	If Hb A_2 is <3.5% in either male or female		Treatment for iron deficience anemia and reevaluation of Hb A_2 and indices after 1 month
9. If Hb A_2 level is between 3.5 and 7.0% in both male and female, the next step should be taken			If indices are normal but Hb A_2 still is <3.5% in either male or female
10. The carrier couple are offered counseling by genetic advisors		If indices are abnormal but still is Hb A_2 <3.5% in either male or female	
11.			DNA analysis and globin chain synthesis studies are conducted

Figure 1. The process by which the National Thalassaemia Prevention Programme is implemented in Iran. (a) Thalassemia screening starts with the male to avoid stigmatization of the woman in a male-dominated society. MCV: mean corpuscular volume; MCH: mean corpuscular Hb.

were provided with expert genetic counseling so that they could make an informed choice, and it was accepted that some couples would decline PND.

Figure 1 shows the different steps of thalassemia prevention in Iran. Thalassemia prevention programs similar to Iran are found in many regional countries including Turkey and Lebanon (10,11). Saudi Arabia has the same screening plan as Iran but PND is not practiced for prevention of thalassemia (12). The necessity of establishing an Iran-like program in other regions with a high prevalence of thalassemia is also felt (13). However, a precise evaluation of the effect of the program on thalassemia affected births is of prime importance.

Samavat and Modell (5) published the first evaluation report on the thalassemia prevention program in Iran. It included the birth rate of new thalassemia cases during 1998–2002, indicating the effect of the program in significantly decreasing new cases (5), which was further validated by the research conducted by Abolghasemi *et al.* (7). However, they did not analyze the fall in affected births in different regions of the country.

Sporadic studies have still been done in different provinces. Khorasani *et al.* (14) reported the registered thalassemic subjects in Bou Alisina Hospital of Sari city (the center of Mazandaran Province located on the North of Iran bordering the Caspian Sea) to be declining from 500 per year in 1993 to an average 35 per year during the years 1995–2005. Nikuei *et al.* (15) have also referred to the success of the program in Hormozgan Province (the Southern province of Iran) by which the rate of newborn β-thalassemia major (β-TM) patients have seriously declined; they emphasize pre marital screening, especially in extended families with the consequent use of PND as an effective measure to control thalassemia in developing countries. Moreover, Ghanei *et al.* (16) conducted a 3-year-long study (January 1993-January 1996) on the primary thalassemia program in Isfahan Province (located in the center of Iran) and showed the success in controlling new β-TM births.

The first comprehensive research evaluating the thalassemia prevention program both country-wide and province-oriented during 2001-2006 was conducted by Hadipour Dehshal *et al.* (17) who had referred to the causes leading to new cases. Based on their report, the average fall in affected thalassemia births of the program during the years of the study was estimated to be 70.38% (17). The above research did not collect data about newborns after 2006 (17) and thus, another study in Iran for the years after was considered to be imperative.

Given the importance of the experience of Iran as a developing Muslim country and its use of premarital screening and PND in decreasing the thalassemia birth rate, the present researchers decided to embark on evaluating the thalassemia prevention program in the years 2007, 2008 and 2009, during which information about new cases of thalassemia was gathered. We intended to estimate the fall in thalassemia affected births in different provinces of Iran and

differentiate at-risk provinces, the ones where the affected births have dropped below 50.0%. The causes of new thalassemia births and the fall in thalassemia affected birth since the program in which couples were offered an informed choice of PND for the control of β-TM were closely evaluated.

Materials and methods

An analytical cross-sectional study was designed to analyze the data of thalassemic subjects born during 2007–2009. Nationality (being Iranian or a foreign citizen), town and province of birth, and the causes of birth were included in the study. The causes of thalassemic births were categorized to be: at-risk couples diagnosed at pre marital screening who declined PND (not using PND), the couples married before 1996 when the thalassemia prevention program officially started (marriage before 1996), newborns to couples married under Sunni religious marriage conventions (prevalent in Sunni regions of Iran) and making delayed marriage registration (unregistered and timeless marriage based on religious conventions), newborns to couples with unregistered time-limited marriage bonds prevalent in the Shiite community (unregistered time-limited religious marriage), newborns to foreign citizens, new cases of β-TM caused by screening errors, new cases of β-TM caused by PND errors, new cases of thalassemia caused by the parents' declining abortion(s), new cases of thalassemia reported too late for abortion (abortion after the religiously permitted less than 5 months of pregnancy), and other miscellaneous causes including *in vitro* fertilization (IVF).

The data of the 3-year study (2007–2009) were collected *via* the Iranian Blood Transfusion Organization (IBTO), Tehran, Iran. The formation of hemovigilance committees in all provincial blood centers of IBTO in 2007 paved the way for access to valid data of thalassemic subjects registered in the country-wide Network of Thalassemia Treatment, active under the supervision of medical universities across Iran. Furthermore, since in Iran there is the likelihood of new thalassemic births caused by PND errors not reported by official sources (17,18), the causes of thalassemic births in different provinces were re-gathered from provincial thalassemia societies. Expected affected births and provincial carrier rates were taken from the database of the Genetic Office of Disease Management Center based at the Iran Ministry of Health, Treatment, and Medical Education (GO-MOH), Tehran, Iran. The data about provincial and nation-wide thalassemia birth rates during 2007–2009 were extracted from the official reports of the Statistical Center of Iran and the statistics of IVF centers in Iran published on the MOH (Ministry of Health) website.

A questionnaire was forwarded to all blood centers of IBTO scattered across 31 provinces of Iran so as to elicit information about the annual new cases of thalassemia and the relevant causes. To receive precise information, the questionnaire was also addressed to 207 thalassemia treatment centers across Iran so as to be filled out by the relevant clinicians. We checked the national ID number of patients and their parents who helped us to preempt the repetitive counts. We tried to adhere to the International Guideline on Ethical Issues in Medical Genetics and Genetics Services (19). Any causes having led to a thalassemic birth were marked ''1'' and any other causes ''0.''

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 the purpose of descriptive statistics, we tried to estimate the fall in affected thalassemic births in the prevention program in Iran both at country and province levels. The fall in β-TM births rate was estimated by the following formula: [1 (observed new thalassemia cases/estimated expectation of new thalassemia cases)] × 100.

Results

Our findings showed that 755 thalassemic subjects were born in Iran during 21 March 2007-21 March 2009 with 274 (out of 939 expected births), 242 (out of 949 expected births), 239 (out of 984 expected births) in the years of 2007, 2008 and 2009, respectively; out of this number, 609 (80.66% of all new cases) were born in seven provinces: Sistan & Baluchestan (with 376 thalassemic subjects accounting for 49.8% of all new cases), Hormozgan, Khuzestan, Kerman, Khorasan, Fars and Mazandaran. The provinces of Sistan & Baluchestan, Hormozgan, Khuzestan, and Kerman had more than 40 new births during the 3 years and are recognized as at-risk regions. Figure 2(A) shows the prevalence of new thalassemia cases in Iran.

Despite the active role the hemovigilance network and provincial thalassemia societies play, the causes of the birth of two thalassemic subjects in Ilam Province are unknown and the cause of another one remains ambiguous. Except for these three cases (0.4% of all reported cases), the causes of the birth of the other 752 newborn thalassemic subjects were carefully reviewed and reported. The main causes leading to new thalassemia births during the 3 years of study, in order of importance, are unregistered and timeless marriage based on Sunni religious conventions, declining PND, marriage before 1996, and screening errors. Table 1 shows the different causes of affected births (2007–2009).

Newborns to foreign citizens, new births to marriages before 1996 or timeless and time-limited unregistered religious marriages, and IVF cases were not covered by the program and were also causes of affected births. Based on our findings, 442 new cases (58.78% of the new births with known causes) were born because they had not been covered by the prevention program. Table 2 shows the coverage scale of the prevention program over the new thalassemia births during the years of the present study.

Our findings also clarified that the annual trend of new thalassemia births since the initiation of the thalassemia prevention program in Iran, has declined from 864 cases in 1996 to 239 in 2009 (the final year of this study). The number of thalassemic newborns in 1997 was estimated to be 741 by Hadipour Dehshal *et al.* (17). This new figure adds up to 766 new cases born in 1997. This failure in registration was not observed in any other years. Figure 3 shows the trend of new thalassemia births from 1996 to 2009.

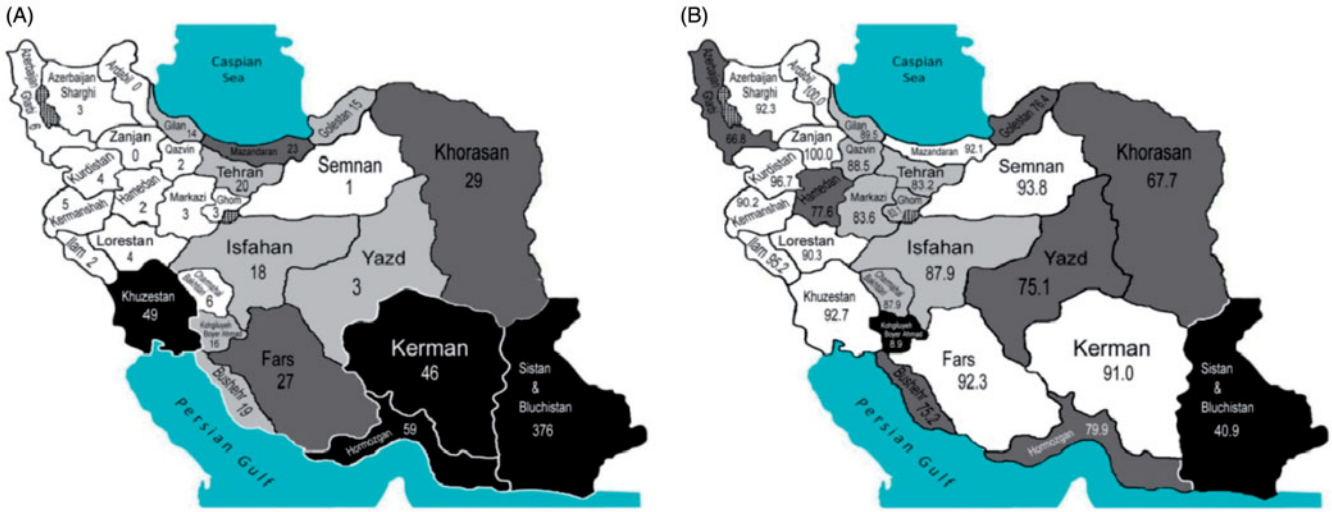

Figure 2. (A) Provincial distribution of new thalassemia cases. (B) Provincial success rates of the National Thalassaemia Prevention Programme (2007–2009).

Table 1. The number of new thalassemia cases in Iran according to different causes of birth and the calculated percentage based on the expected affected birth rate (0.73/1000) (2007–2009).

Causes of new cases	Number of newborns 2007	Number of newborns 2008	Number of newborns 2009	Total number of newborns 2007–2009	Causes in 2007 (%)	Causes in 2008 (%)	Causes in 2009 (%)
Marriage before 1996	37	36	19	92	3.94	3.89	1.93
Refusing PND	85	66	57	208	9.05	6.95	5.79
Unregistered and timeless marriage	108	94	124	326	11.50	9.91	12.60
Unregistered and time-limited marriage	2	0	2	4	0.21	0.00	0.20
Foreign citizens	7	5	6	18	0.75	0.53	0.61
Screening error	22	31	23	76	2.34	3.27	2.34
PND error	5	7	6	18	0.53	0.74	0.61
Refusing abortion	4	0	1	5	0.43	0.00	0.10
In vitro fertilization	1	1	0	2	0.11	0.11	0.00
PND delay	1	1	1	3	0.11	0.11	0.10
Unknown	2	0	0	2	0.21	0.00	0.00
Ambiguous	0	1	0	1	0.00	0.11	0.00

PND: prenatal diagnosis.

Table 2. Number and percentages of newborns with β-thalassemia covered by the Iranian Thalassaemia Prevention Programme (2007–2009).

Year	Total of known cases	Number of newborns not covered by the program (%)	Number of newborns covered by the program (%)
2007	272	155 (56.99)	117 (43.01)
2008	241	136 (56.43)	104 (43.57)
2009	239	151 (63.18)	88 (36.82)
Total	752	442 (58.78)	310 (42.22)

Analysis

Taking into consideration the real observed number of new thalassemia cases in the beginning year of the program in 1996 as the baseline of estimating the affected birth rate, it is expected that 0.73 out of 1000 new births lead to β-TM. This figure depicts the estimated rates of affected births to be 70.82, 74.49 and 75.71% in 2007, 2008 and 2009, respectively; thus, the average fall in thalassemia affected births of the prevention program during the 3 years of the present study was measured to be 73.67%. However, the observed number of new thalassemic births in Iran during 2007–2009 was compared with the rate of affected births theoretically estimated by GO-MOH. Thus, the average success rate of the prevention program in the 3 years of the study was estimated to be 80.82%, with an upward trend of 78.71, 81.38 and 82.28% in 2007, 2008 and 2009, respectively. Figure 3 shows the annual prevented number of new births from the first year of the program to 2009. It should be noted that both baselines of the expected affected birth calculated theoretically by GO-MOH and the affected birth rate estimated based on the number of new β-TM births in the first year of the program in 1996 were used in the diagram.

Although the fall in β-TM births using the expected affected birth rate hypothesized by GO-MOH was 80.82%, however, the average success in Sistan & Baluchestan and Kohgiluiyeh Boyer Ahmad provinces was estimated to be less than 50.0%. Table 3 shows the fall in β-TM births in different provinces of Iran.

Despite the high number of new thalassemic births in Khuzestan, Kerman, Fars and Mazandaran provinces, the

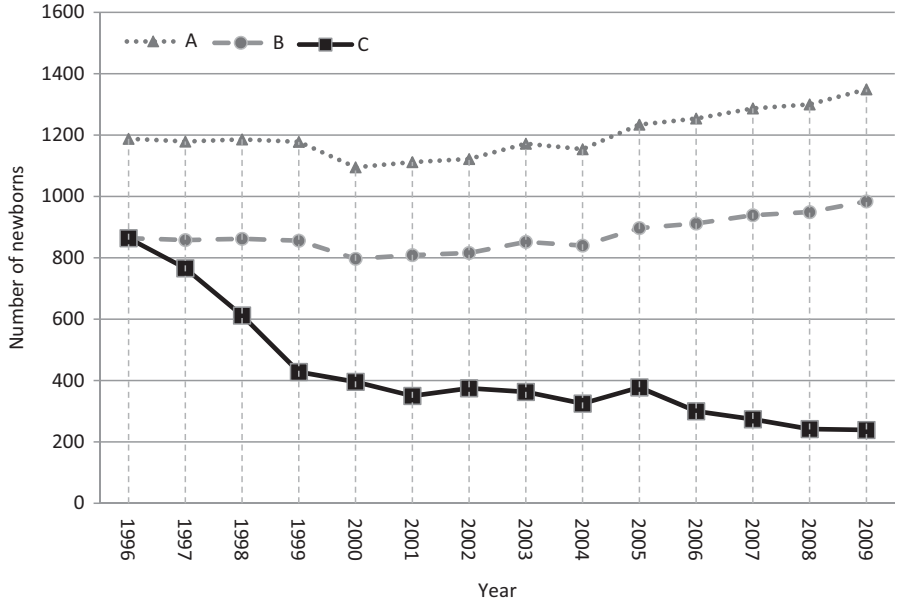

Figure 3. The fall in the rate of thalassemia affected births reported in the Iranian Thalassaemia Prevention Programme (1996–2009). (A) The trend of expected thalassemia affected births per year (considering a rate of 1.00/1000). (B) The trend of expected thalassemia affected births (considering a rate of 0.73/1000). (C) Number of thalassemic births observed.

Tablet 3. Fall in the rate of thalassemia affected births in different provinces in Iran (2007–2009).

Provinces	β-TM births observed in 3 years	Carrier rates (%)	Expected affected births/1000	New births in 3 years	Expected births in 3 years	Fall in affected birth rate (%)
Sistan & Baluchestan	376	8.5	2.7	232,896	629	40.21
Hormozgan	59	9.0	3.0	98,026	284	79.94
Khuzestan	49	7.4	2.3	290,494	668	92.67
Kerman	46	9.5	3.1	165,443	513	91.03
Fars	27	6.7	1.5	233,798	351	92.30
Mazandaran	23	8.0	2.2	131,882	290	92.07
Tehran	20	1.9	0.2	593,865	118	83.16
Bushehr	19	5.7	1.4	54,731	76	75.20
Isfahan	18	4.0	0.7	212,926	149	87.92
Kohgiluyeh Boyer Ahmad	16	2.3	0.4	43,915	18	8.91
Golestan	15	3.9	0.6	106,134	64	76.44
Gilan	14	5.6	1.4	95,287	134	89.52
Azerbaijan Gharbi	6	1.0	0.1	180,455	18	66.75
Charmahal Bakhtiari	6	4.4	0.9	55,291	50	87.94
Kermanshah	5	3.3	0.5	102,340	51	90.23
Kurdestan	4	5.9	1.5	80,795	121	96.70
Lorestan	4	2.6	0.4	103,455	41	90.33
Azerbaijan Sharghi	3	1.7	0.2	195,591	39	92.33
Markazi	3	2.5	0.3	60,933	18	83.59
Ghom	3	2.6	0.3	59,052	18	83.07
Yazd	3	1.5	0.2	60,260	12	75.11
Hamedan	2	1.6	0.1	89,104	9	77.55
Ilam	2	5.9	1.5	29,939	42	95.23
Qazvin	2	2.7	0.3	58,045	17	88.51
Semnan	1	3.6	0.6	26,691	16	93.76
Ardabil	0	2.5	0.2	70,244	14	100.00
Zanjan	0	4.9	0.8	55,451	43	100.00
Khorasan	29	1.7	0.2	450,285	90	67.78
Total	755	1.0	1.0	3935,428	3935	80.82

β-TM: β-thal major.

average fall in β-TM births of more than 90.0% in thalassemia prevention program during the 3 years of the study in these provinces indicate effectiveness. Figure 2(B) shows the average fall in β-TM births in different provinces (2007–2009). By comparing Figure 2(B) with Figure 2(A), we can observe the effect of the program and the new thalassemia cases in each province (2007–2009).

Discussion

There are different viewpoints about the effect of the thalassemia prevention program in different regions of Iran. Furthermore, there is a consensus that the program has been remarkable in decreasing the annual rate of new thalassemic births, even though 239 new cases in the year 2009 showed

there are also aspects of the program that need to be addressed. We have thus decided to consider geographical distribution and the causes of new cases of thalassemia, as previously practiced (17). Our data help decision makers of the health system enhance the program coverage and formulate new strategies, particularly in high-risk provinces.

Samavat and Modell (5) described that the thalassemia prevention program in Iran as very successful in terms of cost-effectiveness with a significant decrease of new thalassemia births. Abolghasemi *et al.* (7) studied the program at different time periods. In their opinion, during the first period from the time the program was officially initiated to the time the religious verdict for time-bound abortion for thalassemia control was issued (1996–1998), no significant fall in β-TM births was observed. The second period was after the abortion verdict was issued, together with access to PND and screening when the program got momentum. Abolghasemi *et al.* (7) also noted the necessity of formulating new strategies for the high-risk province of Sistan & Baluchestan and highlighted the prominence of addressing the new births born to couples married before 1996. Ghanei *et al.* (16) published a report about the pilot implementation of the prevention program in Isfahan Province from 1993 to 1996, during which the number of new thalassemia births reportedly dropped to zero. What we have found about the program from 1996 onward, is that no year without new β-TM births was observed and during the 3 years of the present study (2007–2009), an average number of six new cases had been born annually. These figures are compatible with the reports addressing the years 2001–2006 (17). Khorasani *et al.* (14) asserted that the prevention program has been remarkably successful in Mazandaran, Iran. There is also another report authored by Kosarian *et al.* (20) indicating the rise of awareness and change of attitude and practice among at-risk couples in Mazandaran Province.

Nevertheless, all viewpoints about the thalassemia prevention program are not that positive. Ghotbi *et al.* (21) have emphasized the importance of revisiting the program for the sake of its efficacy. In the study conducted by Miri-Moghaddam *et al.* (22), the ineffectiveness of the program in Sistan & Baluchestan Province has been emphasized. There has been another study by Hadipour Dehshal *et al.* (17) in which, alongside the significant success of the program in Iran, while placing emphasis on the need to formulate a strategy compatible with behaviors and customs of the province of Sistan & Baluchestan and the necessity of program flexibility in provinces with different practices and life patterns.

The research findings of the present study and the assessments made in different provinces during 2001–2006 (17) make it evident that Sistan & Baluchestan and Kohkiluyeh Boyer Ahmad provinces still have a high number of affected births with a 40.0 and 9.0% fall, respectively. Sistan & Baluchestan Province requires a comprehensive and all-embracing reconsideration to be made by the health authority. This province enjoys a differently dominated denomination, and different customs and conventions that affect the relationships among tribe members leading to delay in official marriage registry, and a higher tendency for Baluchis to marry relatives compared to other groups in the country is observed. Furthermore, Baluchi people form a major part of the population of the province; it is adjacent to the Pakistani province of Baluchistan and there are always people who are moving across the common borders (23,24) that should also be taken into consideration. The thalassemia prevention program in Iran is based on couples to officially register their marriage (Figure 1), the program fails to cover conventional region-dominated marriages whose registry are delayed, thereby leading to the birth of 312 cases (82.98% of all new births in the province) during 2007–2009. Three new cases born to foreign citizens and 19 new cases born because of marriages before the year 1996, the program was officially implemented, add to 334 new thalassemia cases (accounting for 88.83% of the total number in the province) during 2007–2009. Thus, a heavy responsibility is placed upon the shoulders of health decision makers to formulate an appropriate and region-compatible program to effectively decrease the thalassemia birth rate in this at-risk province; to this end, they should consult with sociologists and experts involved in and familiar with customs, practices, and life styles of people there. Moreover, the education status of carrier couples and their unawareness about the chances of their giving birth to a child with thalassemia are the factors that should be scrutinized before any decisions are adopted about the prevention program in this province (22). It is evident that any changes according to the religious standards of Sistan & Baluchestan should be based on the offer of informed choice.

The two provinces of Hormozgan (located on the South of Iran) and Khorasan (including Khorasan Razavi, Northern Khorasan, and Southern Khorasan) based on the 2001–2006 (17) evaluation were considered to be high-risk, both in terms of the high annual birth rate and the low average fall in β-TM; however, during 2007–2009 we have seen an increasing fall in β-TM births with an average of 79.94 and 67.78% in Hormozgan and Khorasan, respectively. Still the fall in affected births of the two provinces compared with the average rate of the country are considered low. Moreover, a significant number of thalassemic subjects (59 in Hormozgan and 29 in Khorasan) were born during 2007–2009. Thus, provincial managers bear the responsibility to ensure couples have premarital screening and are offered genetic counseling based on informed choice. To have a better judgment about the growing effect of the prevention program in the above two provinces, further research should be conducted on the years after 2009.

Regarding the four provinces of Kerman, Khuzestan, Fars and Mazandaran, in which thalassemia is highly prevalent, we have been witness to a remarkable success in prevention (Table 3). However, 49 and 46 new birth cases in Khuzestan and Kerman during the present 3-year study could be an impetus for provincial health managers to aim to further evaluate these findings.

Our study shows that 208 new cases were born to couples who were aware of the risk at the screening stage but declined the offer of PND. The reports of the years 2001–2006 show the decrease of the number and the rate of newborns caused by the parents' declining the offer of PND in 2006 (17); this intensifies the hope that the efficacy of the Network of DNA Laboratories be enhanced together with its accessibility to at-risk couples increased. Table 1 shows that the downward

trend of the impact of declining PND cause on new thalassemia births in 2007 compared with 2006 has slowed [2006: 8.44% (17); 2007: 9.05%] but the figures in 2008 and 2009 (6.95 and 5.79%, respectively) still enliven hopes for more access of at-risk couples to PND and the ever increasing efficacy of the Network of DNA Laboratories.

The declining trend of thalassemia births to marriages before 1996 approves the assertion made by Hadipour Dehshal *et al.* (17) about the dispensability of formulating a new strategy for their coverage and refutes that of Abolghasemi *et al.* (7) who did not render such a strategy unnecessary. Out of the total number of newborns during 2007–2009, 76 were caused by screening errors (Table 1). There were a relatively large number of β-TM births due to screening errors. This should act as an incentive for the health authorities to investigate the reasons of the errors and implement safeguards to avoid the same errors in the future. So far no precise statistics on the total screening number of would-be couples across the country and the number of performed PNDs for thalassemia prevention in recent years have been published. In case the aforementioned data are published by GO-MOH, the calculation of the screening and PND error rates in the country would be available to researchers. The findings of the present research display that five new cases were born to parents who had accepted PND but declined termination of an affected pregnancy. One couple declined because they very much wanted a boy, two declined because of pro-life beliefs, and two because of an earlier negative experience of termination. Other methods including preimplantation genetic diagnosis (PGD), can play alternative roles for the pain of repetitive abortions and for those couples who would decline PND (25).

Two of the 755 new thalassemia cases found during 2007–2009 were born to couples using IVF. Given the growing number of IVF centers in Iran, from two in 1991 to 50 in 2011, in future, IVF can change into a negative phenomenon affecting new thalassemic births. Therefore, it should be mandatory for all couples seeking IVF to be screened (26). To further study the birth causes in the provinces with the highest rate of thalassemia during 2007–2009 (6), the effect of each cause was calculated in all provinces (Table 4A and B).

Our findings are compatible with those of the 2001–2006 assessments (17), showing the effect of each cause on new thalassemia births being varied in different provinces. As shown in Table 4 (A and B), during 2007–2009, the most important cause of thalassemic births in Sistan & Baluchestan province has been timeless religious marriages with delay in official registration but in the adjacent province, Hormozgan, it was attributed to screening errors, and in Kerman Province, which neighbors both provinces, it was 'not using PND.'

These differences clearly shed light on the necessity of the prevention program to be changed to be flexible and provincial health decision makers to be entrusted more responsibility to make adjustments in the program to be compatible with the province-wise demands and norms. To this end, sociologists and epidemiologists familiar with relations, conventions, and life styles of different regions of the country can play an important role in raising the efficacy of the program.

Table 4A. The effect of each cause on new births of thalassemia in all provinces (2007–2009).

Provinces	Marriage before 1996 *n* (%)	Not using PND *n* (%)	Unregistered timeless marriage *n* (%)	Unregistered time- limited marriage *n* (%)	Foreign citizens *n* (%)	Screening errors *n* (%)
Sistan & Baluchestan	19 (5.0)	14 (9.0)	312 (83.0)	0 (0.0)	3 (1.0)	6 (2.0)
Hormozgan	5 (8.0)	24 (41.0)	0 (0.0)	0 (0.0)	0 (0.0)	27 (46.0)
Khuzestan	11 (22.0)	33 (67.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)
Kerman	12 (26.0)	19 (41.0)	0 (0.0)	0 (0.0)	1 (2.0)	12 (26.0)
Khorasan	5 (17.0)	14 (48.0)	1 (3.0)	2 (7.0)	2 (7.0)	2 (7.0)
Fars	5 (19.0)	9 (33.0)	1 (4.0)	0 (0.0)	2 (7.0)	6 (22.0)
Mazandaran	4 (17.0)	16 (70.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (13.0)
Tehran	5 (25.0)	6 (30.0)	2 (10.0)	0 (0.0)	4 (20.0)	2 (10.0)
Bushehr	2 (11.0)	12 (63.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (26.0)
Isfahan	7 (39.0)	4 (22.0)	0 (0.0)	0 (0.0)	2 (11.0)	2 (11.0)
Kohgiluyeh Boyer Ahmad	3 (19.0)	8 (50.0)	0 (0.0)	1 (6.0)	0 (0.0)	0 (0.0)
Golestan	3 (20.0)	3 (20.0)	5 (33.0)	0 (0.0)	2 (13.0)	1 (7.0)
Gilan	0 (0.0)	10 (71.0)	0 (0.0)	1 (7.0)	0 (0.0)	1 (7.0)
Azerbaijan Gharbi	1 (17.0)	1 (17.0)	2 (33.0)	0 (0.0)	0 (0.0)	2 (33.0)
Charmahal Bakhtiari	1 (17.0)	5 (83.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Kermanshah	1 (20.0)	4 (80.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Kurdestan	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)
Lorestan	3 (75.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)
Yazd	0 (0.0)	1 (33.0)	0 (0.0)	0 (0.0)	1 (33.0)	1 (33.0)
Markazi	1 (33.0)	2 (67.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Azerbaijan Sharghi	1 (33.0)	0 (0.0)	2 (67.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ghom	2 (67.0)	1 (33.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hamadan	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Qazvin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	1 (50.0)
Ilam	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Semnan	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Zanjan	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ardabil	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

PND: prenatal diagnosis.

Table 4B. The effect of each cause on new births of thalassemia in all provinces (2007–2009) (continued).

Provinces	PND errors *n* (%)	Refusing abortion *n* (%)	*In vitro* fertilization *n* (%)	Unknown *n* (%)	PND delay *n* (%)	Ambiguous *n* (%)
Sistan & Baluchestan	1 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hormozgan	2 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	0 (0.0)
Khuzestan	0 (0.0)	2 (4.0)	0 (0.0)	0 (0.0)	2 (4.0)	0 (0.0)
Kerman	2 (4.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Khorasan	3 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fars	3 (11.0)	0 (0.0)	1 (4.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mazandaran	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tehran	1 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bushehr	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Isfahan	2 (11.0)	0 (0.0)	1 (6.0)	0 (0.0)	0 (0.0)	0 (0.0)
Kohgiluyeh Boyer Ahmad	3 (19.0)	1 (6.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Golestan	1 (7.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gilan	0 (0.0)	1 (7.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (7.0)
Azerbaijan Gharbi	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Charmahal Bakhtiari	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Kermanshah	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Kurdestan	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lorestan	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Yazd	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Markazi	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Azerbaijan Sharghi	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ghom	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hamadan	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Qazvin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ilam	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)
Semnan	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Zanjan	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ardabil	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

PND: prenatal diagnosis.

Limitations

The present research is based on the data registered in the country-wide Iranian National Registration System whose limitations have permeated our study. The worst limitations are the delay and error in registration of new thalassemia cases; therefore, the data covering 2010–2012 were deleted from our present study to avoid false results. We strongly hope that researchers in future would seek the missing information and follow and analyze the trend of new β-TM births in Iran. Moreover, to solve the problem of the lack of access to data about PND errors, non governmental organizations (NGOs) replaced the registration system as the source of information without which it would have been impossible. Yet there were discrepancies between what was provided by the provincial thalassemia societies *vs.* the Haemovigilance System of the country; therefore, the cause of one of the new cases during 2007–2009 has been reported ambiguous.

Samavat and Modell (5) theoretically calculated the expected affected thalassemia births in Iran to be 0.94/1000, while the calculated figure of GO-MOH came out to be 1/1000. Since the former calculation has been based on the data taken from GO-MOH, which then itself modified the data, we considered 1/1000 as the criterion.

Conclusions

It seems that the thalassemia prevention program in Iran has fulfilled its goals in many provinces particularly in thalassemia affected regions. However, the relatively low fall in thalassemia affected births in some provinces should not be overlooked, particularly the two provinces of Sistan & Baluchestan and Kohgiluyeh Boyer Ahmad. In the present study, there are four provinces with more than 40 thalassemic newborns. The findings should raise the awareness of health decision makers and pave the way for proper strategies to be formulated.

The thalassemia prevention program in at-risk provinces, especially in Sistan & Baluchestan and Kohgiluyeh Boyer Ahmad, should be revisited and be put high on the agenda of the health authority, specialty groups of the prevention program, and the NGOs active in prevention of β-TM. For this purpose to be served, health sociologists and epidemiologists should be consulted to find appropriate solutions.

Although the coverage of the Network of DNA Lababoratories has expanded and the access of at-risk couples increased, travel and accommodation expenses for at-risk couples far from laboratories are problematic (17). The GO-MOH can release the total screening number of would-be couples across the country and the number of PNDs performed for thalassemia prevention in recent years so that researchers can calculate the screening and PND error rates in the country. Moreover, the laboratories should be regularly monitored, and PND errors together with the causes should be recorded and analyzed. For those couples choosing PGD in Iran appropriate measures should be taken by the decision makers involved in the thalassemia prevention program.

The evaluation of the trend of new thalassemic births 2009 onward can inform us on the fall in β-TM births in Iran. Thus, efforts should be made for data about new thalassemia cases to be more accessible to researchers to continuously monitor the program outcome. The monitoring together with liberal decision making allowing local committees to make

need-based modifications to the program and make it province-compatible can change the thalassemia prevention program into an appropriate and prominent model for developing countries and the Muslim world.

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Declaration of interest

A declaration of interest statement reporting no conflict has been inserted. Please confirm the statement is accurate.

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