

Evaluation and Cost Analysis of National Health Policy of Thalassaemia Screening in West-Azerbaijan Province of Iran

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ABSTRACT

Background: Thalassaemia is one of the most common Mendelian disorders in Mediterranean area. Iran has about 26,000 Thalassaemic patients, so it is one of the most affected countries. The aim of this study was to evaluate the screening program and cost analysis of Thalassaemia prevention program in West-Azerbaijan province of Iran.

Methods: This study evaluated the efficacy of Health system's Thalassaemia prevention program with a sensitivity analysis for its costs. The second five years of the program was evaluated. The economic burden of Thalassaemia is determined by the birth prevalence of the affected infants and the cost that is accrued to treat the infected individuals and was compared with the total cost of screening the couples for thalassaemia trait.

Results: The average incidence rate of major Thalassaemia was 19.8 per 100,000 live births and mean coverage rate of program was 74%. The rate of canceling the marriage among carrier couples was 53%. Cost analysis showed that the cost of screening and prenatal diagnosis program was much lower than the cost of treatment in potential thalassaemic patients.

Conclusions: The prevention program of Thalassaemia including a premarital and pre-natal screening in west Azerbaijan province is demonstrated to be cost-effective. Taking some actions in order to increase the coverage of pre-marital screening, providing pre-natal diagnosis in private and public sector, complete insurance coverage for the high-risk couples to perform the investigations more easily, were recommended.

Key Words: Cost analysis, Iran, screening, Thalassaemia

INTRODUCTION

Thalassaemia is one of the most common Mendelian disorder in the world.^[1] Thalassaemia is a complicated disease.^[2] Iran is geographically located in the Thalassaemia belt, extending from the Mediterranean basin through the Middle-East, Indian subcontinent, and the Southeast Asia. According to the available

record, number of Thalassaemia cases in this region is well over 150 million cases.^[1,2]

In Iran 26,000 cases of major Thalassaemia have been officially documented,^[3] and the total estimated prevalence of this disorder is 24.91/100,000,^[4] which places Iran in the list of the most affected countries in the world.

Thalassaemia prevention program in Iran

The first screening program for prevention of *Thalassaemia* was initiated in 1991 in the Fars province located in the south of Iran.^[5] The next major screening program formed in 1995 by the joint contribution and efforts of the Iranian Thalassaemia Society and the Iranian Blood Transfusion Organization, where all the high-school students in Tehran, the capital of Iran, were screened for Thalassaemia disorder in cooperation with the local high-schools.^[6] By 1996, under the direction of the genetic department of Centre for Disease Control and Prevention of the Ministry of Health (MOH) and guidance of an academic advisory committee, screening for the identification of this disorder became a national program. The initial national prevention program included: (1) pre-marital screening; (2) counseling parents with thalassaemic children; (3) evaluating the impact of Thalassaemia on individuals who married before the implementation of the national screening program.^[5]

In 2003, genetic counseling for at-risk couples at the time of pregnancy was added to the program. This modification brought about several reforms in abortion-related laws. For example, while abortion for any reason was illegal and prohibited in Iran as a Muslim country but the Islamic clergies declared a *Fatwa* to permit the abortion of homozygote Beta-Thalassaemic fetuses, even after 16 weeks of gestational age. However, the legal abortion was not permitted until 2003. Another protective measure of the program, which led to nearly 80% decrease in the incidence of major Beta-Thalassaemia within the first eight years include prohibition of marriage in couples where both parents were the carriers of Thalassaemic trait.^[7]

Thalassaemia pre-natal screening program in West- Azerbaijan

West-Azerbaijan is located in the north west of Iran neighboring three countries including Iraq,

Turkey, and the Republic of Azerbaijan. In 2006 the province had a population of 3,015,361 people.

The Thalassaemia pre-natal screening program in West-Azerbaijan has used two prong strategies to prevent Major Beta-Thalassaemia; retrospective and prospective. For the retrospective component families who already were known as carriers for Thalassaemia were identified and provided with frequent counseling and education. In the prospective phase, which is depicted in Figure 1, couples who wish to register their marriage are mandated to get premarital certificate. To do so, men are initially screened via blood test. Blood samples are checked for complete blood count (CBC) and red blood cell indices with an automatic cell counter. The premarital certificate is issued if the mean corpuscular haemoglobin (MCH) is ≥ 27 pg and the mean corpuscular volume (MCV) is ≥ 80 fl. Otherwise, the blood sample of the couple will be studied with column chromatography to determine the level of hemoglobin (HbA_2).

Individuals with an $HbA_2 \geq 3.5\%$ but $< 7\%$ are considered as the carriers and subsequently receive genetic counseling. Couples with $HbA_2 < 3.5\%$ undergo a treatment trial with iron supplements. During the follow-up test if these couples, despite the iron therapy, present with $HbA_2 < 3.5\%$ and a normal electrophoresis, or the $HbA_2 > 7\%$, they will

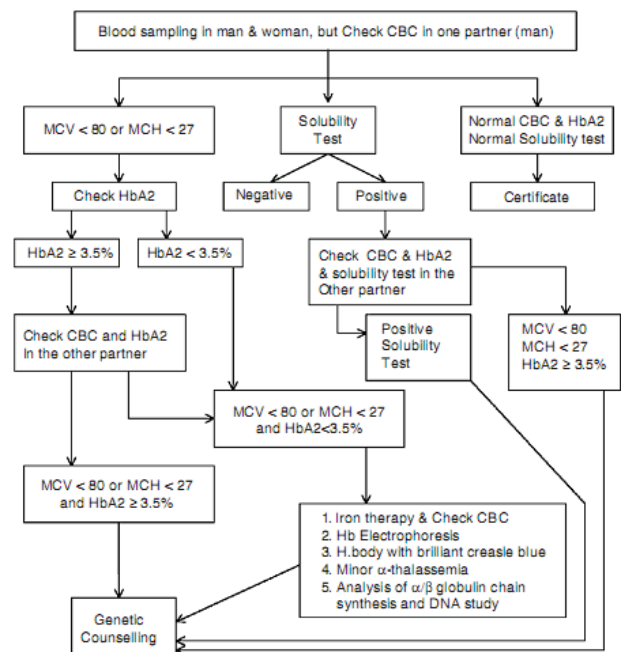


Figure 1: Pre-natal screening program in Iran

be scheduled to received further tests (i.e. cellulose acetate electrophoresis at PH 8.4 for Hbs, HbG, HbE, Hbc and σ/β -Thalassaemia differentiation). The disease and its consequences and possible options (including canceling the marriage, or proceeding with the marriage plan while accepting not to conceive a child) are then discussed with each of the carrier couples. On the other hand, couples who decide to go forward with the marriage plans and happen to conceive a child will receive prenatal screening and are offered elective abortion in cases where fetus is affected. Currently, there are only two genetic counseling centres in Iran. One located in Tehran and the other in Fars, a province in the Southern region of Iran. Both centres are far from the West-Azerbaijan province, therefore, couple's access to prenatal screening for thalassaemia is limited.

Some evaluations demonstrated the prenatal screening for Thalassaemia to be cost-effective.^[8-10] In Cyprus, the annual cost of screening and prenatal diagnosis program was found to be almost equal to the cost of treatment of all existing patients for five years.^[11]

Considering the different results of cost analysis in different settings, in this study we aimed to evaluate the cost-effectiveness of the Thalassaemia pre-natal screening program that has been took place in this province since 1996.

METHODS

The conduct of this study was approved by the Scientific Review Board of Urmia University of Medical Sciences, Iran. Data for the evaluation of the second phase (Prenatal screening) of the program (2002-2006) was obtained from the Centre for Disease Control and Prevention (CDC) of the Ministry of Health Office.

The program evaluation measures

The following measures were used for program evaluation:

Incidence rate of Thalassaemia per year:

$$\frac{\text{Number of Homozygote} - \beta \text{ Thalassaemala}}{\text{Number of birth}}$$

The percentage of program coverage:

$$\frac{\text{Number of screened couples}}{\text{Number of registered couples}}$$

Effectiveness of counseling:

$\frac{\text{Number of refusal couples}}{\text{Number of carrier couples}}$

General cost-effectiveness of the program:

$\frac{\text{Cost difference (with and without program)}}{\text{Difference in the birth rate of Homozygote-}}$

β (with and without program)

The economic burden of Thalassaemia is determined by the birth prevalence of the affected infants and the cost that is accrued to treat the infected individuals, to the point where they can be a healthy functioning member of the society. This cost was compared with the total cost of implementing the prevention program (conducting laboratory tests, etc.) among couples to detect the thalassaemia trait.

In this paper, descriptive and sensitivity analysis were used to provide a cost analysis of a Thalassaemia prevention program in West-Azerbaijan for the period between 2002-2006. Sensitivity analysis was applied for cost evaluation and the descriptive analysis was used for other items.

RESULTS

According to the Centre for Disease Control and Prevention of the Iran's Ministry of Health (MOH), 112 patients with Major Thalassaemia have been registered until 2006. Of these patients, 46 (41%) were diagnosed/identified after the introduction of the Thalassaemia prevention program. The program's minimum coverage rate was reported at 63% in 2003 and its maximum coverage reached 90% in the year 2006. The mean coverage rate was 74% [Figure 2].

For the same period (2002-2006), the average rate of marriage cancellation among the carrier couples was reported at 53%, with the minimum rate of 38% in 2003 and the maximum rate of 69% in 2006 [Figure 3].

Moreover, the average annual incidence rate of major Thalassaemias reported at 19.8 cases per 100,000 live births with the highest rate being 28/100,000 live births during 2003 [Figure 4]. The 10-year incidence rate of major Thalassaemiasince the introduction of the Thalassaemia prevention program in West-Azerbaijan was 46 cases of which

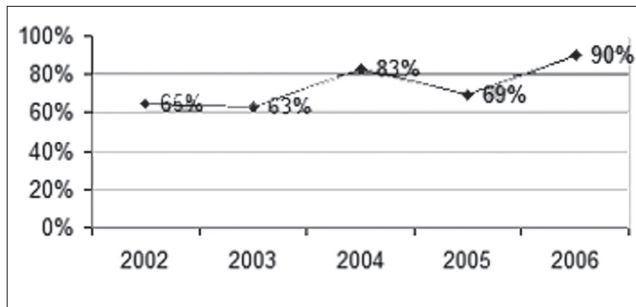


Figure 2: Program coverage rate in Iran (2002-2006)

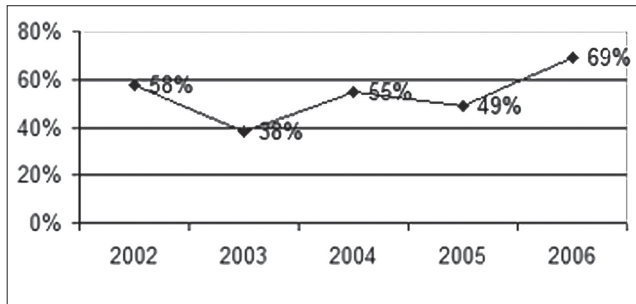


Figure 3: Rate of canceling marriage among Iranian carrier couples

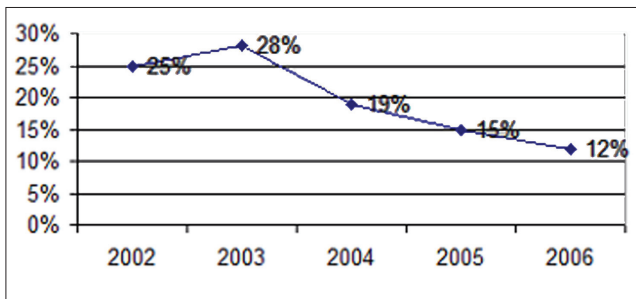


Figure 4: The incidence rate of major Thalassaemia per 100,000 live births (2002-2006)

32 (70%) were born during the first five years of the Thalassaemia prevention program.

Due to the lack of availability of the prenatal diagnostic (PND) test for major Thalassaemia in West-Azerbaijan province the suspected individuals were directed to the referral centres (Tehran). Only six couples received the genetic counselling and none of them undergone CVS (Chorionic villus sampling). Of the six couples, only one affected fetus with major Thalassaemia (17%) was detected, which subsequently was aborted once legal permission was obtained.

The life-time cost of optimum treatment in developed countries has been estimated about 1,350,000 USD (un-subsided) per patient.^[12] This includes the cost of blood transfusions,

Table 1: The estimate cost of treating a Thalassaemia patient in Iran

Item	Cost in USD
Blood sampling	0.95
Pre-marital counseling	3.5
Hb electrophoresis	7.2
Genetic counseling	778
Optimum treatment/year	6,500
Lifelong treatment	100,000

medications, the essential treatments, hospital care and home visits. Thalassaemic patients receive red blood cell transfusions every 2-3 weeks, amounting to approximately 24.6 liters of blood a year. In Iran, 50-60% of all donated blood is used for blood transfusion therapy in Thalassaemic patients. Each bag of blood costs the country's Blood Transfusion Organization at least 25 USD.

Desferrioxamine is not manufactured in Iran and importing a 500mg vial of the drug costs about 3 USD. A 12-year-old, 30kg patient treated with regular blood transfusion requires three vials daily throughout his life. This, in addition to the cost of disposable syringes and scalp-vein needles, which is about 3,360 USD per year and the cost of infusion pump, which is about 400 USD, adds up to approximately 3,760 USD per case, annually. Very few people can afford receiving optimum care, therefore, considering that government-funded healthcare coverage is limited, many thalassaemic patients die immaturely.^[13-15] Table 1 depicts the estimate cost of treating a Thalassaemia patient.

Considering that the cost of providing optimum care for a thalassaemic patient can add up to 6,500 USD per year -based on the aforementioned data, therefore the cost of care for 46 such patients can escalate to approximately 300,000 USD annually, and 3 million USD for a ten-year program. On the other hand, the cost of preventing similar cases based on the aforementioned data, would roughly add up to 4600 USD. In addition, it is estimated that 235 cases could have been prevented just by conducting screening program and couple consulting. Considering the costs provided by MOH, the total cost of caring for 235 cases could catch up to 15,275,000USD in 10 years.

During first ten years of implementation of the thalassaemia screening program, almost 44,500 people in Urmia, were screened for thalassaemia

before the marriage. This costs almost 4,450,000 USD which should be added to the above mentioned three million dollars (the cost of optimum care for 46 thalassaemia cases occurred against the implementation of prevention program). According to the sensitivity analysis, 7,825,000 USD was saved during ten years since 1997 until 2006 by preventing 235 major thalassaemia cases to be occurred.

DISCUSSION

We found that the total cost of preventing one case of Thalassaemia (100 USD) is less than a single year of optimum treatment for a case with major Thalassaemia (6500 USD). Furthermore, the cost of screening the population (44,500 people) in addition to the cost of optimum care for the 46 major Thalassaemia patients (i.e. those who were born against the implementation of the prevention program) can reach up to 7,450,000 USD which is extremely lower than the cost of optimum care for 235 potential thalassaemia cases who may be born in the absence of prevention program. Thus the thalassaemia prevention program is demonstrated to be quite cost-effective.

All the new cases of Thalassaemia (46 cases) in the period between 1996-2006 were identified in patients with family history of Thalassaemia. Of the new cases, one couple were referred for genetic testing. This couple were married a year prior to the initiation of the program and were worried about having a child with major Thalassaemia. Although the result of their genetic test showed no risk of major Thalassaemia, their child became a major case. Parents' non-compliance with the recommended prevention measures is often responsible for the new cases of major Thalassaemia. These are parents who lack access to appropriate health insurance to cover the cost of PND tests. In West-Azerbaijan PND is not yet available to every family suggesting a need to prioritize access to comprehensive health insurance at least to all the at-risk parents in this region. Currently, only a few health care plans offer comprehensive coverage for screening and diagnosis of Thalassaemia to the at-risk families, but couples have to travel to the capital (i.e. Tehran) to receive the tests.

Evaluation reports from other countries in

the region have shown similar findings. The Thalassaemia prevention screening program has been successful in Cyprus where screening is mandatory although prenatal diagnosis is optional.^[11] In Turkey, the results of a four-year premarital screening program demonstrates that the counseling services for the carrier couples, the prenatal diagnosis, and the termination of pregnancy in cases of an affected fetus were successful in preventing major Thalassaemia.^[16,17] Similar prevention measures have resulted in successfully curbing Thalassaemia in Saudi Arabia.^[18] In these countries, except in Cyprus, at-risk couples are mandated by law to call off their weddings.^[11]

In Northern Sardinia, due to appropriate education, compliance for the prenatal diagnosis increased from 87% to 96%.^[19] A report from Italy notes an increase in PND among couples with minor Thalassaemia. Subsequently, 24.8% of these couples screened positive with major Thalassaemia. This study reported 2.2% spontaneous abortion and 2.7% preterm labor. There were no significant relationship between sampling for PND and such outcomes.^[20] In our study, only one couple was identified with major Thalassaemia via PND. They eventually aborted the pregnancy by seeking legal permission. No complication was reported after the procedure.

CONCLUSION

In conclusion, the Thalassaemia prevention program including a premarital and pre-natal screening has been cost-effective in West-Azerbaijan province of Iran. This study demonstrates that the costs of detection of high-risk couples or an affected fetus and termination of pregnancy are quite cheaper than the cost of full treatment of a major Thalassaemia case.

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