ORIGINAL ARTICLE

Assessing the Success and Effectiveness of the Major β-Thalassemia Screening Program in Southeast Iran: A Case Study of Jiroft District

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Abstract

Background: Major β-Thalassemia is the most prevalent single-gene disorder in Iran. Over 2 million beta-thalassemia carriers and more than 25,000 patients have been identified nationwide. This study aimed to evaluate the Major β-Thalassemia (MBT) screening surveillance system in the Jiroft district, southeast Iran.

Methods: This descriptive study was conducted using the census method and was based on the information recorded in the files of all major thalassemia births (born between 2011 and 2021) in the health centers of Jiroft University of Medical Sciences. A formula was used to calculate the program's incidence, expected incidence, and success rate. Stata version 14 and Excel software were utilized to analyze the data, and the qualitative data are presented as numerical values and percentages.

Results: During the study periods, 91 patients with beta-thalassemia Major were born in the population covered by Jiroft University of Medical Sciences. By performing prenatal diagnosis tests in the first weeks of pregnancy and obtaining parental consent for legal abortion, the birth of 422 sick children was prevented. The 11-year incidence of beta-thalassemia major was 5.32 per 10,000, and the expected incidence (if no prevention program was implemented) was 30 per 10,000 live births. The mean success rate of the Major β-Thalassemia surveillance system during the study period was 82.26%, which reached 95.45% in 2021.

Conclusion: The implementation of efficient, effective health policies influenced by the native culture of the region has resulted in the thalassemia prevention program in Jiroft City being completely effective. The implementation success rate of this program has exceeded 95%. Modeling and adapting these preventive policies can assist in implementing thalassemia prevention programs in other parts of the country and developing countries.

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Introduction

Thalassemia is a genetic disorder that impairs the production of hemoglobin in the blood, leading to anemia.[1] The disorder, named after the Greek words for sea and blood, is most prevalent in regions such as the Mediterranean, North and West Africa, the Middle East, India, and Southeast Asia.[2, 3]

The average incidence of Major β-Thalassemia (MBT) in Eastern Mediterranean countries, including Turkey, Cyprus, Syria, Israel, Lebanon, and Palestine, is estimated to be 3.14 per 10,000[3]. Beta-thalassemia carriers are estimated to number around 80 million worldwide, and low or middle-income countries account for 90% of the approximately 23,000 annual births of babies with MBT globally. Countries such as Cyprus (12-15%), Greece (7.4%), Turkey (2.1%), and Arab countries (1-11%) have the highest prevalence of beta-thalassemia minor in the Mediterranean region.[4]

Beta-thalassemia is the most prevalent single-gene disorder in Iran, with over 2 million carriers and 25,000 patients identified in the country.[5, 6] Thalassemia minor is more common in Iran than the global average, estimated at 4-8%. In some provinces, it reaches 10%, posing significant challenges to the success of thalassemia prevention programs in these regions.[2, 7, 8] Jiroft, located in southeast Iran, has a high prevalence of thalassemia. The disease rate varies across different regions of the city and is higher in the southern areas of the province.[6]

Untreated beta-thalassemia primary patients usually die before age five if not diagnosed before birth. Symptoms include stunted growth, anemia, enlarged liver and spleen, muscle weakness, and skeletal changes. Thalassemia patients are also at risk of HIV, hepatitis C, and B infection and may develop osteoporosis.[9, 10]

The Centers for Disease Control and Prevention of the Ministry of Health and Medical Education (Iran) aims to reduce the number of major births of beta-thalassemia in Iran through the national program to prevent its occurrence since 1997. This program involves three strategies. The first strategy requires thalassemia minor screening for all couples before marriage and counseling and dissuasion for those with both partners affected. The second strategy involves screening during pregnancy and following up with the approved flow chart to prevent beta-thalassemia major births. The third strategy involves identifying and screening thalassemia carrier couples who married before 2016.[11]

The thalassemia prevention program is a crucial and long-standing program in the healthcare system aimed at preventing new disease cases.[12] Marriage screening, genetic counseling, prenatal diagnosis, and care programs are currently being implemented in Iran to prevent the birth of patients with thalassemia major.[13, 14] The program has resulted in an 80% reduction in cases of thalassemia major in the country, preventing at least 10,000 patients. The incidence of the disease has dropped from 1000 to less than 200 cases per year. However, new cases are still reported, especially in high-prevalence areas like Sistan and Baluchistan, Khuzestan, Hormozgan, and Jiroft.[14]

Studies in Iran have shown that the leading cause of new cases of beta thalassemia major after the implementation of prevention programs is the marriage of parents before the start of the screening program and lack of carrier information. Other factors include errors in genetic testing and screening, issues with the disease care system, insufficient follow-up, delayed PND tests, and inadequate counseling services.[12, 15]

This study aims to investigate and analyze the causes of beta thalassemia majors in the cities affiliated with Jiroft University of Medical Sciences from 2011 to 2021.

Methods

Study Design

This descriptive study was conducted using the census method based on the information recorded in the files of all major thalassemia births (born 2011-2021) at the Jiroft University of Medical Sciences Health Center. All necessary information was extracted from the national form used for examining the occurrence of genetic diseases, focusing on data related to premarital screening, history of gene care, and the cause of disease occurrence. The study's inclusion criteria encompassed all Iranian patients with a confirmed diagnosis of MBT, whose information was registered in the health center affiliated with Jiroft University of Medical Sciences and who had a file in the Jiroft Blood Transfusion Center.

Measures

The following formulas were used to calculate the incidence, expected incidence, and success rate of the program:

Incidence: (number of identified patients/ number of births in the same year) *10000.

Expected incidence: (number of identified patients + number of aborted beta-thalassemia patient fetuses/ number of births in the same year) *10000.

Success rate: (number of aborted fetuses of the patient/number of born patients + number of aborted fetuses of the patient) *100.

Genetic Care Process

Based on the screening test results, couples diagnosed as definite carriers of thalassemia or suspected high-risk couples are introduced to the care team at the health care centers by the genetic counselor. These couples are cared for and followed up during the fertility period until the completion of the family with healthy children. Initially, couples are referred to the program's selected genetic diagnosis laboratory to determine the type of gene mutation. Chorionic Villus Sampling (CVS) is performed on the fetus from

10 to 14 weeks during each pregnancy. If the fetus is diagnosed with a problem, it is the responsibility of the parents to decide on the abortion of the fetus. After a comprehensive consultation, if abortion is chosen, the parents are referred to forensic medicine to confirm the diagnosis and obtain the abortion license. If the procedure is confirmed to be legal, the couple will be referred to the desired hospital for abortion.

Statistical Analysis

Data were analyzed using Stata version 14 (Stata Corp LP, College Station, TX) and Excel software. Qualitative data are presented as numbers and percentages.

Results

According to the information in Table 1, during 2011-2021, 91 patients with beta-thalassemia Major were born in the population covered by Jiroft University of Medical Sciences. By performing prenatal diagnosis tests in the first weeks of pregnancy, after obtaining parental consent for legal abortion, the birth of 422 sick children was prevented. The 11-year incidence of beta-thalassemia major was 5.32 per 10,000, and the expected incidence (if no prevention program was implemented) was 30 per 10,000 live births.

As shown in Figure 1, the incidence has decreased over the years studied, and a significant difference was observed between the incidence and the expected incidence. According to Table 2, the incidence in Ghaleganj cities (10.48 per 10,000) was higher than in other cities.

The success rate in most covered areas was above 80%, and in the whole area, it was 82.26%. The success rate of the program in Qalaganj city was lower than in other regions (70.83%), and in Kohnuj city, it was higher than in other cities (91.56%) (Table 2).

Based on the information recorded in the files of thalassemia patients, the causes of this disease were divided into three categories: 1) causes related to the process of identifying carrier couples, 2) causes associated with the genetic diagnosis process, 3) causes related to the genetic care process (Table 3).

Table 1: Frequency, incidence, expected incidence, and success rate of Major beta-thalassemia prevention program during 2011-2021

Year	Observed TM Births	Incidence per 10,000	Expected incidence per 10,000	Total Births	Expected TM Births	Aborted	Success Rate (%)
2011	13	8.68	26.1	14961	39	26	66.66%
2012	16	10.10	27.8	15836	44	28	63.3%
2013	17	9.83	34.1	17293	59	42	71.18%
2014	10	5.40	18.9	18509	35	25	71.42%
2015	11	6.22	17.5	17668	31	20	64.51%
2016	5	2.87	25.8	17419	45	40	88.88%
2017	8	5.12	26.9	15620	42	34	80.95%
2018	5	3.43	35	14554	51	46	90.19%
2019	2	1.48	41.5	13489	56	54	96.42%
2020	2	1.56	52.3	12814	67	65	97.01%
2021	2	1.58	34.8	12630	44	42	95.45%
Total	91	5.32	30.03	170793	513	422	82.26%

TM: Thalassemia Major

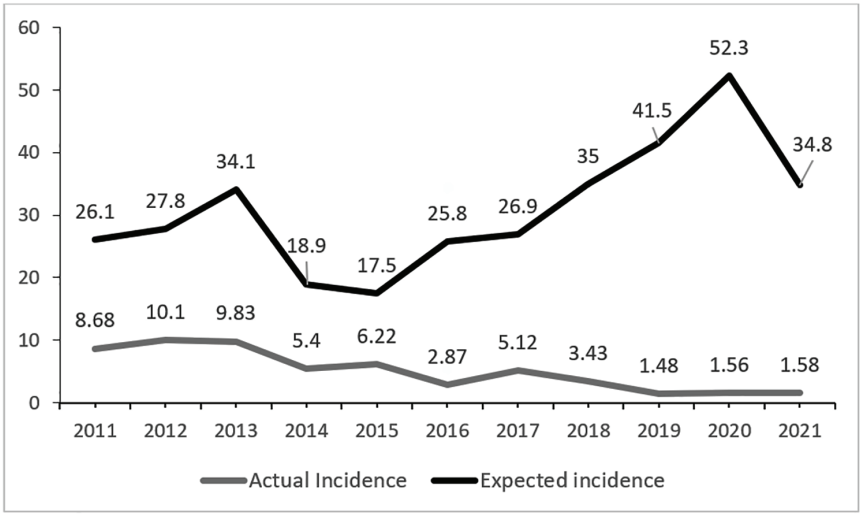

Figure 1: Comparison of the actual and expected incidence (Per 10,000 population) of beta-thalassemia major in the population covered by Jiroft University of Medical Sciences between 2011 and 2021.

Table 2: Frequency of incidence, expected incidence, and success rate of the Major beta-thalassemia prevention programs by regions

Location	Observed TM Births	Incidence per 10000	Total Births	Expected TM Births	Therapeutic abortion	Success Rate (%)
Jiroft	25	5.08	49169	117	92	78.63%
Anbarabad	9	4.57	19659	59	50	84.74%
Kahnooj	7	2.34	29829	83	76	91.56%
Ghalegnaj	21	10.48	20034	72	51	70.83%
Roudbar	19	5.70	33285	114	95	83.33%
Manoojan	7	4.99	14028	43	36	83.72%
Faryab	3	6.26	4789	25	22	88%
Total	91	5.32	170793	513	422	82.26%

Table 3: Incidence of thalassemia by causes

Actions	Incidence of thalassemia by causes		Frequency	Percent
Identification process	Unofficially marriage		20	22%
	Failure to identify couples getting married before the screening program		5	5.5%
	Mistakes in premarital screening or pnd1 test		9	10%
Genetic diagnosis process	Non-identical fetal and parental mutations		6	6.5%
Genetic care process	Did not do the PND test or abortion	PND	34	37%
		Abortion	11	12%
	Failure to detect pregnancy in time		6	7%
Total			91	100%

PND: Prenatal Diagnosis

Discussion

This study was conducted to retrospectively analyze the incidence of MBT over the last decade in the cities affiliated with Jiroft University of Medical Sciences. The target population in this study included all beta-thalassemia major babies in the areas covered by Jiroft University of Medical Sciences between 2011 and 2021.

This study investigated the quality of implementing the national program to prevent thalassemia in the south of Kerman province (Jiroft city). In other words, the higher the quality of the implementation of the mentioned program, the closer the number of beta-thalassemia births will be to zero, and the success rate will be closer to 100%.

The results show that implementing the thalassemia prevention program in the southern region of Jiroft City has been successful over the past 11 years. Although the number of births has not reached zero, thalassemia births have decreased from 13 cases in 2011 to 2 in 2021. The success rate increased from 66% in 2011 to 95.45% in 2021, and during this period, 422 thalassemia patients were prevented from being born.

The increasing trend of the success rate can be divided into two periods: before and after 2016. After this year, the success rate reached over 80%, with a significant jump, and this rate reached more than 97% by 2020. So, only six patients were born during the three years from 2019 to 2021. The results show that since 2016, the implementation of specific health policies has improved the quality of the thalassemia prevention program.

In this study, the average incidence of MBT during the last decade (cumulative incidence) was estimated to be 5.32 per 10,000. The incidence trend during the previous decade has been significantly decreasing, decreasing from 8.68 per 10,000 in 2011 to 1.58 per 10,000 in 2021, which means that more than 80% of the incidence has been reduced in a decade.

The results of Giambona's study in Sicily,[16] Italy, also showed that the implementation of the thalassemia prevention program caused the incidence of MBT (41 per 10,000 before the performance of the prevention program) to decrease by more than 85% after about three decades of the implementation of the prevention program in 2015. The prevalence of thalassemia carriers in the mentioned region is estimated to be 8%, similar to the Jiroft region in this respect. The results of the Ladis's study in Greece also show a decrease in the incidence of thalassemia major in three decades after the start of the prevention program by more than 81%, which is similar to the present study.[17]

In Iran, the study of Samavat and Model was the first research investigating the implementation adequacy of the thalassemia prevention program during the first five years after its start (1998-2002) in Iran. Without the program's implementation, expected births were estimated to be around 1200 people per year. The results showed that thalassemia births decreased and reached 78 cases in 2002.[11] The reason for the previous report was the delay in birth registration.[18] Miri's study determined that the number of thalassemia births in 2014 decreased to 239 cases in the country. The success rate of implementing the prevention program until 2009 was estimated to be more than 82%.[18] Different provinces of the country have not been evaluated equally. This issue has been

more pronounced, especially in the case of regions such as Kohgiluyeh Boyer Ahmad and the Southeast of the country.[19]

The results of the study by Ghorbani Aliabadi and colleagues in Jiroft City show that the incidence of thalassemia births between 2001 and 2015 was much higher than in other provinces despite the decreasing incidence in the region. More than half of the thalassemia children were born between 2006 and 2015.[20] Meanwhile, a study in Fars province showed that the success of implementing the prevention program in 2011 led to only 2 cases of thalassemia births in Fars province, which has a population of nearly 5 million people.[21] our study has also confirmed the significant jump in the success of the thalassemia prevention program in Jiroft city, especially from 2016 onwards. About 73.5% of thalassemia children in this study were born between 2011 and 2015. In the last three years leading to 2021, annual births have reached only 2.

This study divides MBT occurrence factors into three categories according to causes (Table 3). The first and most important cause of MBT, which includes more than half (56%) of the causes of thalassemia births, are factors related to the genetic care process. These are caused by the non-cooperation of pregnant mothers or families to perform PND2 (37%), lack of cooperation to perform abortion treatment (12%), or failure to recognize pregnancy on time (7%). According to the recorded information, the main factors that led to not doing PND2 were the non-cooperation of pregnant mothers, lack of consent of husbands (cultural poverty), fear of sampling, and lack of proper understanding of complications. In connection with the non-cooperation for the abortion treatment that led to the birth of 11 thalassemia children, factors such as fear due to the history of previous abortions, financial poverty, maternal love and guilt for the abortion, hope for healing by prayer writers and inhibiting religious beliefs, it had led to non-cooperation.

In connection with the failure to recognize pregnancy in time, the religious fatwa in Iran should be mentioned that if the diagnosis of MBT is confirmed during the PND2 test, abortion treatment will be allowed only before 18 weeks.[22] During pregnancy, followed by failure to perform PND2 before 18 weeks was the cause of occurrence (7%) of MBT cases in this study.

Although the incidence of thalassemia births has decreased significantly after 2016, according to the current study, the first and most important factor in the incidence of thalassemia is the factors related to the genetic care process, i.e., failure to perform PND2 and Abortion has been a treatment in such a way that during six years ending in 2021, this factor accounted for 16 out of 24 cases (66.6%) of thalassemia births.

Notably, in the study of Rezabeighi in Kerman, the main factor in the incidence of thalassemia births was the lack of identification of thalassemia carrier couples.[23] Still, in the present study, the main incidence factor is different.

The second reason for the occurrence of MBT in this study, which included (37.5%) of the causes, was the factors related to the identification process, which had children from informal and unregistered marriages (22%), children from spouses before the implementation of the prevention program (5%), and births resulting from errors in the screening process and Prenatal diagnosis (PND1) (10%).

The current study mentioned that informal and unregistered marriages were the second cause of MBT births. In this regard, it is essential to note that the highest and lowest percentages of success in implementing the prevention program belonged to the cities of Kohnouj (91.56%) and Qalaganj (70.83%), respectively. In Qalaganj city, the population of Sunnis is higher than in the other areas under our study. As a result, the number of unofficial and unregistered marriages in this region is higher than in other places; therefore, due to the cultural differences caused by Religion, the necessary cooperation to implement the prevention program in this region has been less than in other places. Previous studies at the national level have also shown that in Sunni areas, especially in the Southeast of the country, such as Sistan and Baluchistan, informal and unregistered marriages have been the primary cause of MBT in these areas.[18, 22, 24] For instance, in a study by Miri Moghadam in 2012 in Sistan and Baluchistan province, 80% of the thalassemia patients under study resulted from informal and unregistered marriages (the leading cause of incidence) in the region. More than 70% of the couples were unaware that they were carriers of thalassemia.[25] Previous studies have paid particular attention to this significant occurrence factor, especially in areas with Sunni populations, such as the country's Southeast. In planning, Ati has found it necessary to adjust the thalassemia prevention program based on cultural norms in these areas.[19]

In the current study, the number of children born from unofficial and unregistered marriages has declined to zero in the four-year period ending in 2021. The last instance of this occurrence was in 2017 when 2 out of 8 cases (25%) were attributed to the annual birth rate of thalassemia. Therefore, the apparent success of preventive policies and executive solutions concerning this emerging factor has been evident in the region under study in recent years.

Lastly, the third factor related to the genetic diagnosis process involved non-identical mutations

in the fetus and parents, which accounted for 6.5% of the causes in this study.

The significant decrease in thalassemia births from 2016 onwards in Jiroft city can be attributed to the measures taken by the Health Deputy. In the last five years, various actions have been implemented. The following can be mentioned among the most critical measures:

1- Organizing committees to analyze the causes of occurrence and provide related interventions.

2- Educating, raising awareness, and changing attitudes in target groups and key people of society (Friday imams, local religious leaders, head marriage registrars, students, and young people on the verge of marriage).

3- Enlisting the participation of clerics to cooperate and gain people's satisfaction.

4- Setting up two new laboratories equipped with electrophoresis devices.

5- Allocating allowances to poor couples and providing vehicles and guest houses to accommodate teams in the province's center to perform genetic diagnosis tests.

6- Using the capabilities of psychological experts in health networks.

7- Launching campaigns to identify couples without thalassemia screening tests before marriage in the context of pre-pregnancy care.

8- Intra-departmental coordination with the family and school population health group to improve the index of coverage of pre-pregnancy services to reduce the age of pregnancy detection and strengthen monthly genetic care.

9- Setting up a sample transfer system to the genetic diagnosis laboratory to prevent couples from not cooperating due to lack of financial resources or distance.

This study does have certain limitations. First, the small sample size could affect the results' generalizability to other regions or countries with different cultural, social, and economic backgrounds. Second, measurement errors are possible, particularly in terms of the accuracy of implementing the thalassemia screening program and the reliability of diagnosing beta-thalassemia major cases.

Conclusion

Implementing efficient and effective health policies in line with the region's native culture has resulted in the highly effective execution of the thalassemia prevention program in Jiroft City. The success rate of this program's implementation has exceeded 95%. Modeling and adapting these preventive policies could potentially enhance the implementation of the thalassemia prevention program in other parts of the country and developing countries.

Despite the apparent success of these policies, the primary cause of MBT incidence in the region after 2016 is related to the genetic care process, particularly the non-cooperation of pregnant mothers and their families in performing Prenatal Diagnosis (PND2) or abortion treatment. In this context, a broader and more effective implementation of the current preventive policies could likely be effective and potentially reduce the incidence to zero.

Ethical Permissions

The study protocol was in accordance with the ethical principles of the Helsinki Declaration and was approved by the Jiroft University of Medical Sciences's Research Ethics Committee. The Institutional Review Board (IRB) approved the study protocol under the reference number IR.JMU.REC.1400.028.

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Authors' Contribution

EGH and SD conceived and designed the study. AK and BK undertook the literature search and screening. SR and VR were in charge of data collection and analyses. SD and EGH contributed to data interpretation. AK, BK, and SR drafted the manuscript, while VR critically revised the manuscript.

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References

1 Li C-K. New trend in the epidemiology of thalassaemia. Best Practice & Research Clinical Obstetrics & Gynaecology. 2017; 39:16-26. doi: 10.1016/j.bpobgyn.2016.10.013; PMID: 27847257.

2 Karimi M, Emadmarvasti V, Hoseini J, Shoja L. Major causes of hospital admission in beta thalassemia

major patients in southern Iran. Iranian journal of pediatrics. 2011;21(4):509. PMID: 23056840; PMCID: PMC3446139.

3 Bellis G, Parant A. Beta-thalassemia in Mediterranean countries. Findings and outlook. Investigaciones Geográficas. 2021(in press):1-10. doi: 10.14198/INGEO.19079.

4 De Sanctis V, Kattamis C, Canatan D, Soliman AT, Elsedfy H, Karimi M, et al. β-thalassemia distribution in the old world: an ancient disease seen from a historical standpoint. Mediterranean journal of hematology and infectious diseases. 2017; 9(1). doi: 10.4084/MJHID.2017.018; PMID: 28293406; PMCID: PMC5333734.

5 Rezaee AR, Banoei MM, Khalili E, Houshmand M. Beta-Thalassemia in Iran: new insight into the role of genetic admixture and migration. The Scientific World Journal. 2012;2012. doi: 10.1100/2012/635183; PMID: 23319887; PMCID: PMC3539370.

6 Saleh-Gohari N, Bazrafshani M. Distribution of β-globin gene mutations in thalassemia minor population of Kerman Province, Iran. Iranian journal of public health. 2010;39(2):69. PMID: 23113009; PMCID: PMC3481756.

7 Miri M, Tabrizi Namini M, Hadipour Dehshal M, Sadeghian Varnosfaderani F, Ahmadvand A, Yousefi Darestani S, Manshadi M. Thalassemia in Iran in last twenty years: the carrier rates and the births trend. Iranian Journal of Blood and Cancer. 2013;6(1):11-7. URL: http://ijbc.ir/article-1-432-en.html.

8 Dehbozorgian J, Moghadam M, Daryanoush S, Haghpanah S, Imani fard J, Aramesh A, et al. Distribution of alpha-thalassemia mutations in Iranian population. Hematology. 2015;20(6):359-62. doi: 10.1179/1607845414Y.0000000227; PMID: 25553732.

9 Lai K, Huang G, Su L, He Y. The prevalence of thalassemia in mainland China: evidence from epidemiological surveys. Scientific reports. 2017;7(1):920. doi: 10.1038/s41598-017-00967-2; PMID: 28424478; PMCID: PMC5430438.

10 Helmi N, Bashir M, Shireen A, Ahmed IM. Thalassemia review: features, dental considerations and management. Electronic physician. 2017;9(3):4003. doi: 10.19082/4003; PMID: 28461877; PMCID: PMC5407235.

11 Samavat A, Modell B. Iranian national thalassaemia screening programme. Bmj. 2004;329(7475):1134-7. doi: 10.1136/bmj.329.7475.1134; PMID: 15539666; PMCID: PMC527686.

12 Zeinalian M, Samavat A, Fadayee Nobari R, Azin S. Incidence rate of major beta-thalassemia and study of its causes after prevention and control program of thalassemia in Isfahan Province. Scientific Journal of Iranian Blood Transfusion Organization. 2009;6(4):238-47. URL: http://bloodjournal.ir/article-1-365-fa.html.

13 Akhlaghpoor S. Chorionic villus sampling for beta-thalassemia: the first report of experience in Iran. Prenatal Diagnosis: Published in Affiliation with the International Society for Prenatal Diagnosis. 2006;26(12):1131-6. doi: 10.1002/pd.1572; PMID: 17009347.

14 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):263-71. doi: 10.1080/03630260802004269; PMID: 18473242.

15 Zeinalian M, Moafi A, Fadayi-Nobari R. A study to evaluate the results of pre-marital screening program for beta-thalassemia in Isfahan province, 1997-2010. Scientific Journal of Iran Blood Transfus Organ. 2013;10(1):20-30. URL: http://bloodjournal.ir/article-1-736-fa.html.

16 Giambona A, Damiani G, Vinciguerra M, Jakil C, Cannata M, Cassara F, et al. Incidence of haemoglobinopathies in Sicily: the impact of screening and prenatal diagnosis. International Journal of Clinical Practice. 2015;69(10):1129-38. doi: 10.1111/ijcp.12628; PMID: 25727926.

17 Ladis V, Karagiorga-Lagana M, Tsatra I, Chouliaras G. Thirty-year experience in preventing haemoglobinopathies in G reece: achievements and potentials for optimisation. European journal of haematology. 2013;90(4):313-22. doi: 10.1111/ejh.12076; PMID: 23331260.

18 Hadipour Dehshal M, Ahmadvand A, Yousefi Darestani S, Manshadi M, Abolghasemi H. Secular trends in the national and provincial births of new thalassemia cases in Iran from 2001 to 2006. Hemoglobin. 2013;37(2):124-37. doi: 10.3109/03630269.2013.772062; PMID: 23470148.

19 Hashemieh M, Naghadeh HT, Namini MT, Neamatzadeh H, Dehshal MH. The Iran thalassemia prevention program: success or failure? Iranian journal of pediatric hematology and oncology. 2015;5(3):161. PMID: 26705456; PMCID: PMC4688601.

20 Ghorbani Aliabadi E, Kiani A. Investigating the causes of Beta Thalassemia after start of prevention program in Jiroft city during 2001-2015. Journal of Jiroft University of Medical Sciences. 2019;6(1):168-77. URL: http://journal.jmu.ac.ir/article-1-222-en.html.

21 Joulaei H, Shahbazi M, Nazemzadegan B, Rastgar M, Hadibarhaghtalab M, Heydari M, et al. The diminishing trend of β-thalassemia in Southern Iran from 1997 to 2011: the impact of preventive strategies. Hemoglobin. 2014;38(1):19-23. doi: 10.3109/03630269.2013.858638; PMID: 24274135.

22 Hadipour Dehshal M, Tabrizi Namini M, Ahmadvand A, Manshadi M, Sadeghian Varnosfaderani F, Abolghasemi H. Evaluation of the national prevention program in Iran, 2007–2009: the accomplishments and challenges with reflections on the path ahead. Hemoglobin. 2014;38(3):179-87. doi: 10.3109/03630269.2014.893530; PMID: 24669933.

23 Rezabeigi Davarani E, Mohseni Takaloo F, Vahidnia A, Daneshi S, Rezabeigi Davarani M, Khanjani N,

et al. Epidemiological Investigation of a Twenty-Year Major β-Thalassemia Surveillance in Kerman, Iran. Archives of Hygiene Sciences. 2020;9(4):265-74. doi: 10.52547/ArchHygSci.9.4.265.

24 Hadipour Dehshal M, Tabrizi Namini M, Hantoushzadeh R, Yousefi Darestani S. β-Thalassemia in Iran: things everyone needs to know about this disease. Hemoglobin. 2019;43(3):166-73. doi: 10.1080/03630269.2019.1628774; PMID: 31272240.

25 Miri-Moghaddam E, Naderi M, Izadi S, Mashhadi M. Causes of new cases of major thalassemia in sistan and balouchistan province in South-East of iran. Iranian journal of public health. 2012;41(11):67. PMID: 23304678; PMCID: PMC3521888.