

Appropriateness of Congenital Hypothyroidism Screening Program in Fars Province, Iran: A Retrospective Study from 2005 to 2015

Soheila Shaghaghian¹, MD; Nazila Rahimi², MSc; Razieh Sadat Mousavi-Roknabadi³, MD; Fatemeh Azadian⁴, BSc; Behnam Nazemzadegan², MD; Hamidreza Ghasempour⁵, MD; Mohsen Moghadami⁴, MD; Soheila Keshavarz¹, MD

¹Communicable Diseases Unit, Shohada-e-Enghelab Health Center, Shiraz University of Medical Science, Shiraz, Iran;

²Non-Communicable Diseases Unit, Health Chancellor of Shiraz University of Medical Science, Shiraz, Iran;

³Department of Community Medicine, Faculty of Medicine, Shiraz University of Medical Science, Shiraz, Iran;

⁴Non-Communicable Disease Research Center, Shiraz University of Medical Science, Shiraz, Iran;

⁵Shohada-e-Enghelab Health Center, Shiraz University of Medical Science, Shiraz, Iran

Correspondence:

Soheila Keshavarz, MD;
Communicable Diseases Unit, Shohada-e-Enghelab Health Center, Sibooye Boulevard, Postal code: 7164788363, Shiraz, Iran

Tel: +98 71 37381011

Fax: +98 71 37387723

Email: keshavarz.soheila@yahoo.com

Received: 04 July 2018

Revised: 08 October 2018

Accepted: 04 November 2018

What's Known

- Primary congenital hypothyroidism (CH) may lead to irreversible complications.
- The complications can be prevented if diagnosis and treatment are timely through screening.
- Since 2005, the screening program has been integrated into the health system of Iran.

What's New

- The coverage of neonatal CH screening program in Fars province has increased (2005-2015).
- The coverage of screening in the age of 3-5 days has increased.
- The prevalence of neonatal CH has increased from 0.0126 to 0.0258.
- The percentage of treatments that were started at the optimal age has increased.

Abstract

Congenital hypothyroidism (CH) may lead to irreversible mental retardation. To prevent the complication, screening was conducted routinely for all neonates in Iran. This study aimed to evaluate the appropriateness of CH screening programs in Fars province, southern Iran. This retrospective study (February–May, 2017) was conducted in the Health System Research Center of Shiraz University of Medical Sciences (SUMS). The data were obtained from the non-communicable diseases' unit of SUMS regarding congenital hypothyroidism screening of all neonates born in Fars province from 2005 to 2015. We evaluated the coverage of CH screening, the incidence rate of CH, the percentage of the neonates screened for CH in ideal time, and neonates with CH treated in appropriate time. Descriptive statistics were used to determine the indices. To compare the incidence rate of boys and girls, we used Chi-square test. The coverage of CH screening in Fars Province increased from 50.0% in 2005 to 99.7% in 2015. Furthermore, the percentage of the neonates screened in the ideal time and the neonates with CH treated in an appropriate time increased from 26.0% and 78.0% in 2005 to 86.6% and 99.7% in 2015, respectively. In the evaluated period, the coverage of CH screening in Fars province (98.1%) was higher than that of the other provinces of Iran (83.0%). The study showed good screening coverage in Fars Province from 2005 to 2015. The coverage was considerably better than other provinces of Iran and improved during the study period. Also, over the course of time, more neonates were screened in an ideal time and treated in the appropriate time.

Please cite this article as: Shaghaghian S, Rahimi N, Mousavi-Roknabadi RS, Azadian F, Nazemzadegan B, Ghasempour HR, Moghadami M, Keshavarz S. Appropriateness of Congenital Hypothyroidism Screening Program in Fars Province, Iran: A Retrospective Study from 2005 to 2015. *Iran J Med Sci.* 2019;44(3):245-250. doi: 10.30476/IJMS.2019.44980.

Keywords • Congenital hypothyroidism • Mass screening • Neonatal screening • Iran

Introduction

Primary congenital hypothyroidism (CH) refers to low levels of thyroid hormones in the neonate's blood, which may lead to irreversible complications such as mental retardation and deafness.¹ CH of any cause is difficult to be recognized within the neonatal period, because of normal gross appearance.² The complications can be prevented if diagnosis and treatment are timely through screening; this timely diagnosis and treatment has already found to greatly reduce the socioeconomic burden

of the disease.³ In 1993, CH screening was recommended by the American Academy of Pediatrics.⁴ Today, screening is done routinely in most countries of the world,⁵ and various studies have been conducted to examine the status of CH screening program.⁶⁻⁸

In Iran, a pilot study was conducted about CH screening in 1987, and it was discontinued because of iodine deficiency. The program was started again from 1997.⁶ Since 2005, the program has been integrated into the health system and has gradually been implemented in all provinces. All provinces have been covered by this program since 2007. The prevalence of CH was reported as 1:914 live births in Tehran and 1:357 in Isfahan.^{7, 8} Also, studies showed that this program was cost-effective.⁹

Although Fars is one of the largest provinces in southern Iran, the status of neonatal CH screening programs has not been investigated in it. Therefore, this study was aimed to evaluate the appropriateness of neonatal CH screening programs in Fars province and compare it with that of other provinces of Iran.

Materials and Methods

According to congenital hypothyroidism guideline from Ministry of Health and Medical Education of Iran,¹⁰ from 2005, all neonates born in Fars Province should be screened regarding CH. The results of the screening were archived in non-communicable diseases' unit of Shiraz University of Medical Sciences (SUMS).

In this retrospective study (February-May, 2017), using the archived data, we evaluated the screening of all neonates born in Fars province, Iran (2005- 2015). However, stillbirth neonates and the neonates whose names were not recorded in the National Organization for Civil Registration of Iran were excluded from the study. We obtained the number of the screened neonates and their age at the screening time, and the number of the infants diagnosed to suffer from CH and their age at the onset of treatment from the non-communicable diseases' unit. Furthermore, information about all neonates born in Fars province from March 2005 to March 2015 was obtained from the National Organization for Civil Registration of Iran. Because the existed data were categorized according to Iranian calendar, the data of the neonates born from first to last day of 1384 Hijri Shamsi (21 March 2005-20 March 2006) were recorded as the data belonging to 2005. The data belonging to other years were also categorized in the same fashion.

To evaluate the appropriateness of CH

screening, we evaluated the following indices:

- The coverage of CH screening: The screened neonates for CH in Fars Province per 100 neonates born in the province, based on the information obtained from the National Organization for Civil Registration of Iran.

- The incidence rate of CH: The number of neonates diagnosed to suffer from CH per 100,000 neonates screened in a year.

- The percentage of the neonates screened for CH in an ideal time (3rd-5th day of lives), in an acceptable time (6th-21st day of lives), and in an undesirable time (22nd day of lives or later)

- The percentage of the infants who were suffering from CH and their treatment was started in an appropriate time (27th day of lives or before), in an acceptable time (28th-40th day of lives), and in an undesirable time (41st day of lives or later)

In addition, we compared the coverage of CH screening in Fars Province with that of the other provinces of Iran. The coverage in the other provinces of Iran was calculated according to the national reports existing in the non-communicable diseases' unit.¹¹

Data were analyzed using SPSS version 21.0 for Windows. We used descriptive statistics to determine the indices. To compare the incidence rate for boys and girls, Chi-square test was used ($\alpha=0.05$). Microsoft Office Excel version 2013 for Windows was used to create the diagrams. The study was approved by the local Research Ethics Committee (#14463). To consider ethical issues, the collected data were not revealed to anybody, except to the researchers; therefore, the patients' names were kept confidential.

Results

Based on the Registered Office statistics (2005 and 2015), 787,995 infants were borne in Fars Province. Based on the registered statistics in the non-communicable diseases unit of SUMS, 98.9% (773,066) of the infants were screened for neonatal hypothyroidism, of which 376,827 (48.74%) and 396,239 (51.26%) were girls and boys, respectively. As figure 1.a shows, the screening coverage had increased rapidly over the years. Currently, 99.7% of infants born in Fars province are screened. Moreover, the coverage of screening in Fars province was higher than that of other provinces of Iran during all these years (figure 1.b).

All 1,691 infants with neonatal hypothyroidism (862 girls and 829 boys) had been diagnosed during these years. Therefore, out of every 100,000 newborns in Fars province, 218.74 newborns had neonatal hypothyroidism.

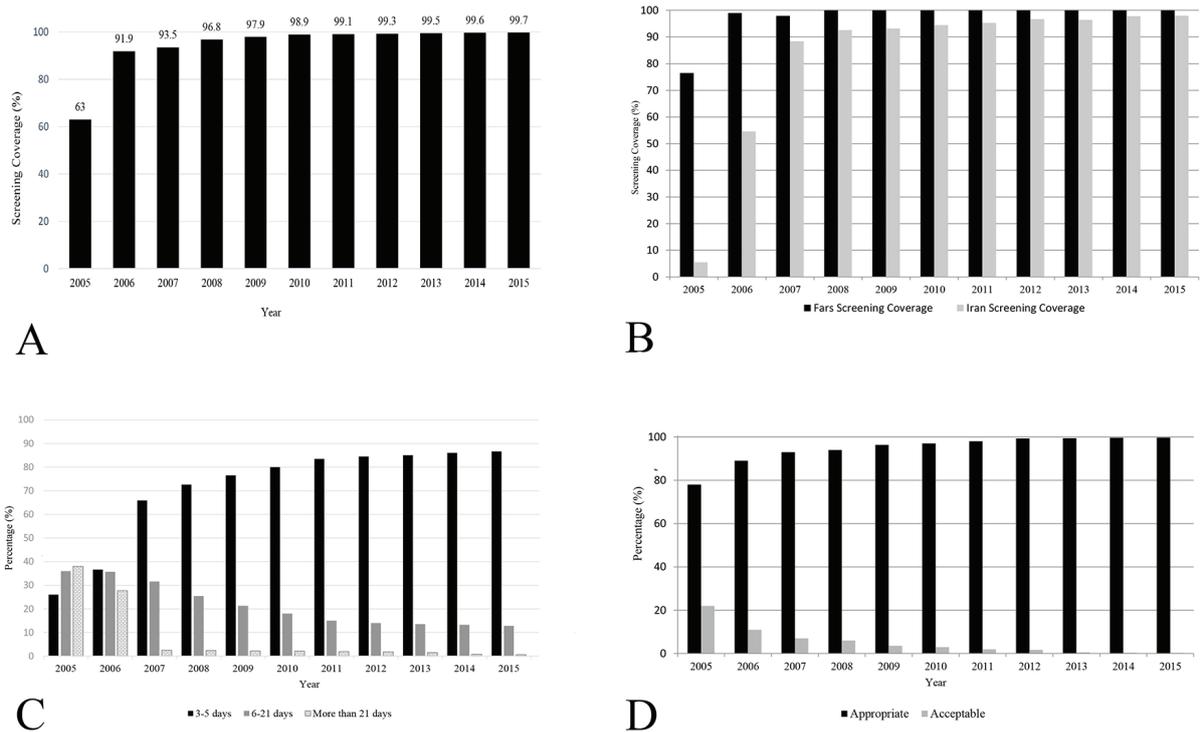


Figure 1: The figures indicate the evaluations of appropriateness of congenital hypothyroidism screening program in Fars province, Iran (2005-2015). A) The coverage of neonatal congenital hypothyroidism screening program in Fars province increased rapidly since 2005 up to 2015. B) The coverage of neonatal congenital hypothyroidism screening program in Fars province was higher than other provinces of Iran from 2005 to 2015. C) The percentage of the neonates who were born in Fars province and for whom congenital hypothyroidism screening program was conducted in an appropriate time increased over the specified years. The screening in an unacceptable time decreased rapidly. D) The percentage of neonates who were born in Fars province, diagnosed as congenital hypothyroidism, and treated in an appropriate time increased rapidly from 2005 to 2015.

There was no significant difference between the incidence of the disease in two genders (incidence rate per 100,000 infant, 228.75 for girls vs. 209.22 for boys, $P=0.066$) (table 1). From 2005 to 2015, the percentage of the neonates screened in an ideal time is shown in figure 1.c.

In these years, all infants who had been diagnosed with neonatal CH had been treated, generally at a favorable or acceptable time. Only for two infants, one in 2007 and one in 2008,

the treatment had started in an unacceptable time. The percentage of newborns that started receiving treatment at the optimal time increased in these years so that in 2014, 99.7% of the infants received the treatment at the optimal time (figure 1.d).

Discussion

Overall, the coverage of the screening, which elevated rapidly during the evaluated period,

Table 1: Incidence of neonatal congenital hypothyroidism in Fars province (2005-2015)

Year	The number of newborns screened	Number of infants with neonatal hypothyroidism	The incidence of neonatal hypothyroidism (for 100,000 screened neonates)
2005	50000	126	252.00
2006	64385	131	203.46
2007	67648	107	158.17
2008	70355	119	169.14
2009	73232	120	163.86
2010	74344	120	159.27
2011	76255	134	175.73
2012	74629	167	223.77
2013	72192	182	252.10
2014	74383	227	305.18
2015	74643	258	345.64
Total	773066	1691	218.74

was good and better than that of the other provinces of Iran. Moreover, the percentage of the neonates screened in an ideal time and treated in an appropriate time increased rapidly in the period mentioned and reached a good level.

In our study, although only about 63% of the newborns were screened for CH in 2005, the coverage of the screening reached 99.7% in 2015. This showed that Fars province made acceptable progress in implementing this program. Also, compared with the national reports,¹¹ the coverage of screening in Fars province had been higher than that of other provinces of Iran during the years investigated in this study. The reason for not reaching 100% screening coverage was out-reach populations including tribal neonates and those who were born in prison. Thus, it is necessary to plan to facilitate screening programs for these two groups of populations.

Comparing the CH screening coverage in Fars province with that of all provinces of Iran, we found better coverage in Fars province in all years of the study period. In our study, the incidence rate of CH was 228.75 per 100,000 infant for girls and 209.22 per 100,000 infant for boys, with no significant difference between the two. The proportion of boys to girls was 1:1.4 in Tehran province,¹² and 0.7 in Isfahan province.⁸ A study showed that there was no statistically significant correlation between gender and the prevalence of the disease, as well as the level of Thyroid-stimulating hormone (TSH).¹²

This study showed that the incidence rate of CH had increased from 2.6 in 2005 to 3 in 2015. This rate was 0.4% in a study in Tehran.¹² Although the definitive cause of this increase has not been identified, it has been suggested that 36% to 38% of the national increase could be accounted for by changes in demographic characteristics among live births, including race, ethnicity, gender, birth plurality, birth weight, and mother's age.¹³

The prevalence of neonatal CH was estimated at 0.0126 in 2005, which increased to 0.0258 in 2015. The prevalence of CH varies in different parts of the world. It has been reported 1:2326 in Turkey and 1:1823 in Lebanon.^{14, 15} The results of other studies showed a prevalence of 1:1002 in Tehran and 1:289 in Yazd.^{7, 16} The causes of the prevalence and the increase in the occurrence of the disease are:

1. Increased screening coverage,
2. Improved laboratory procedures,
3. Increased attention paid to the neonates of special conditions (premature, weigh <2,500 or >4,000 gr, two or more hospitalized, history of

specific medications, blood transfusions),

4. Reported iodine deficiency in food. Causes of iodine deficiency in Fars province are lack of access to seafood, mountainous region, and iodine deficiency in salt and improper use of salt from iodine. The goal of optimizing the access of pregnant mothers to iodine is recommended from the third month before pregnancy to the fourth month of pregnancy.¹⁶

Our study showed that the time of CH screening in Fars province improved over time. Although 38% of neonates were screened in an undesirable time in 2005, about 80% of the neonates were screened in an ideal time in 2015. The following reasons could have contributed to this improvement:

1. Coordination between the Registry Office, where the issuance of ID is only possible when the screening document is shown. This action was taken in the early years of the program, yet after the general education of the community and raising awareness about the importance of screening since 2009, this requirement was removed.

2. Increased access to screening centers in the province.

3. Stabilization of the experts in the province as to reduce sampling error.

4. Training the pregnant women about the importance of screening in the first and second months of pregnancy.

5. Implementation of the screening regulations for hospitalized neonates with emphasis on neonates who were neonatal intensive care unit (NICU)-registered.

The goal of neonatal screening for CH is to ensure that affected neonates start treatment as soon as possible, and not later than within the first 2 weeks of life, to prevent or minimize neurological impairment. Although in 2005, the treatment started for only 87% of the neonates suffering from CH in an appropriate time, in 2015, 99.7% of them received their treatment in an appropriate time. This indicator shows the desirability of the program because the golden time for CH treatment and to have enough time to perform diagnostic confirmatory tests is before 28 days. Thus, it is better that the first sampling be done within 3-5 days. The main reasons for improving this index are as follows:

1. Ease of access to screening centers in the province;

2. Targeted training of health-care workers, pregnant mothers, and the general public;

3. Effective and compassionate follow up procedures;

4. Appropriate care context.

This was a retrospective study and we used

the data available to us, so it is possible that the data were not properly recorded, but we tried to minimize this problem by exact data recovery. Although the coverage of the screening program was high, the incidence rate was not exactly 100% due to the percentage of neonate which had not been screened. However, because of high coverage, the rate was near the exact rate.

Conclusion

The coverage of the screening program in Fars province was considerably higher than the whole of Iran during the implementation of the program. To achieve complete screening, we need to increase access to those neonates who are born in tribes and prisons. The prevalence and incidence of CH has increased due to the increased screening coverage and improved laboratory procedures. The percentage of neonates whose treatments started at the time of optimal age had increased during the period of time which this study was focused on and this showed the success of this screening program in Fars province for that period.

Acknowledgment

The authors would like to thank the Research Chancellor of SUMS for his financial support, and the Health Chancellor (Grant No. 14463) and Non-communicable Diseases' Unit of SUMS for sharing the data with authors.

Conflict of Interest: None declared.

References

- Bellman SC, Davies A, Fuggle PW, Grant DB, Smith I. Mild impairment of neuro-otological function in early treated congenital hypothyroidism. *Arch Dis Child*. 1996;74:215-8. PubMed PMID: 8787425; PubMed Central PMCID: PMC1511406.
- Buyukgebiz A. Congenital hypothyroidism clinical aspects and late consequences. *Pediatr Endocrinol Rev*. 2003;1:185-90. PubMed PMID: 16444157.
- Iran Ministry of Health and Medical Education. National Screening for congenital hypothyroidism and TSH transient. [Accessed September 27, 2018]. Available from: <http://dayyerhc.bpums.ac.ir/UploadedFiles/xfiles/%D8%AF%D8%B3%D8%AA%D9%88%D8%B1%D8%A7%D9%84%D8%B9%D9%85%D9%84%20%20%D9%87%DB%8C%D9%BE%D9%88%D8%AA%DB%8C%D8%B1%D9%88%D8%A6%DB%8C%D8%AF%DB%8C.pdf>. Persian.
- American Academy of Pediatrics AAP Section on Endocrinology and Committee on Genetics, and American Thyroid Association Committee on Public Health: Newborn screening for congenital hypothyroidism: recommended guidelines. *Pediatrics*. 1993;91:1203-9. PubMed PMID: 8502532.
- LaFranchi SH. Worldwide coverage of newborn screening for congenital hypothyroidism—a public health challenge. *US Endocrinol*. 2014;10:115-6. doi: 10.17925/USE.2014.10.02.115.
- Azizi F. Screening for congenital hypothyroidism: Late start but promising. *Iranian Journal of Endocrinology and Metabolism*. 2004;6:1-3.
- Ordookhani A, Mirmiran P, Walfish PG, Azizi F. Transient neonatal hypothyroidism is associated with elevated serum anti-thyroglobulin antibody levels in newborns and their mothers. *J Pediatr*. 2007;150:315-7. doi: 10.1016/j.jpeds.2006.11.034. PubMed PMID: 17307555.
- Hashemipour M, Hovsepian S, Kelishadi R, Iranpour R, Hadian R, Haghghi S, et al. Permanent and transient congenital hypothyroidism in Isfahan-Iran. *J Med Screen*. 2009;16:11-6. doi: 10.1258/jms.2009.008090. PubMed PMID: 19349525.
- Rahmani K, Yarahmadi S, Etemad K, Mehrabi Y, Aghang N, Koosha A, et al. Importance of Early Treatment in Congenital Hypothyroidism. *Iran J Pediatr*. 2017;27:e9438. doi: 10.5812/ijp.9438.
- Yarahmadi SH, Ajang N [Internet]. National Program of congenital hypothyroidism screening. [Accessed September 27, 2018]. Available from: <http://www.health.gov.ir/ncdc/Glands/ch/DocLib/finalTkarshenas.pdf>
- National Progress Report of infants' hypothyroidism screening program, Food and Metabolic Diseases Office, Disease Management Center. Iran Ministry of Health Publication, 2004.
- Najafian B, Shahverdi E, Afsharpaiman S, Shohrati M, Karimi S, Konjedi MA. Neonatal Screening for Congenital Hypothyroidism in an University Hospital in Tehran, Iran. *Journal of Comprehensive Pediatrics*. 2016;7:e34500. doi: 10.17795/compreped-34500.
- Olney RS, Grosse SD, Vogt RF, Jr. Prevalence of congenital hypothyroidism—current trends and future directions: workshop summary. *Pediatrics*. 2010;125:S31-6. doi: 10.1542/peds.2009-1975C. PubMed PMID: 20435715.

- 14 Simsek E, Karabay M, Safak A, Kocabay K. Congenital hypothyroidism and iodine status in Turkey: a comparison between the data obtained from an epidemiological study in school-aged children and neonatal screening for congenital hypothyroidism in Turkey. *Pediatr Endocrinol Rev.* 2003;1:155-61. PubMed PMID: 16444153.
- 15 Daher R, Beaini M, Mahfouz R, Cortas N, Younis KA. A neonatal screening in Lebanon: Results of five years' experience. *Ann Saudi Med.* 2003;23:16-9. PubMed PMID: 17146215.
- 16 Noori Shadkam M, Jafarizadeh M, Mirzaei M, Motlagh M, Eslami Z, Afkhami M, et al. Prevalence of congenital hypothyroidism and transient increased levels of TSH in Yazd Province. *SSU_Journals.* 2008;16:315-22.