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Original

The incidence of congenital hypothyroidism in neonates born in Chaharmahal and Bakhtiari province from 2015 to 2021; A cross-sectional study

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Abstract

Introduction: Congenital hypothyroidism (CH) is one of the most common endocrine and metabolic disorders and a common preventable cause of mental retardation across the world. This disorder can be prevented if diagnosed and treated before the age of four weeks.

Objectives: This study was performed to investigate the incidence rate of CH in infants in Chaharmahal and Bakhtiari province.

Patients and Methods: The data of this study were obtained by the CH screening program from 2015 to 2021 in the health deputy of Chaharmahal and Bakhtiari province.

Results: A total of 651 patients were diagnosed with CH, which showed an incidence rate of 5.06 per 1000 births (1 per 198 live births) in the province. The highest incidence of the disease was obtained in 2016 and the lowest incidence in 2021. Lordegan city had the highest incidence rate (8.1 per 1000 live births) and Kiar had the lowest one (1.67 per 1000 live births) during the study period. Moreover, the highest and lowest incidence rates in terms of season were observed in winter and summer, respectively.

Conclusion: It can be concluded that Chaharmahal and Bakhtiari province, especially Lordegan, is one of the regions with high prevalence of CH in Iran, therefore the incidence rate is not only higher than the national average but also higher than the global average. Hence, the potential causes of this observation deserve further investigation.

Keywords: Incidence, Congenital hypothyroidism, Screening, Neonatal

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Introduction

Congenital hypothyroidism (CH) refers to thyroid hormone deficiency at birth (1,2). This disease is one of the most common endocrine and metabolic disorders and a common preventable cause of mental retardation across the world (3,4). This disorder can be prevented if diagnosed and treated before the age of four weeks (5-7). The symptoms of this condition include decreased activity, lack of proper weight gain, enlargement of the anterior fontanelle, and violent crying (8).

The disorder is divided into permanent and transient types; the transient type heals spontaneously, while the permanent type necessitates medication for the rest of life. The transient type is mainly caused by iodine disorders in the mother during pregnancy or exposure of the baby to high levels of iodine during or after birth (9). Thyroid hormones are necessary for the normal growth and development of the nervous system. The critical period of the central nervous system's dependence on thyroid hormones is from the embryonic period to at least the first two years of life (7,8). Most infants with CH appear to be normal because the placental transfer of maternal thyroid hormone and an increase in iodothyronine deiodinase [converting thyrotoxin (T4) to iodothyronine (T3)] in the brain compensates for the hormonal deficiency (10).

The incidence of CH varies depending on various factors such as screening method, gender [the incidence of the disorder is about twice higher in girls than in boys (11)], birth weight, ethnicity, age, consanguineous marriage, type of delivery and birth order (12) and race (relatively higher in Asia) (11,13). In terms of season, the highest incidence of CH has been reported in autumn and

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winter. A study in Isfahan, in the central Iran showed the highest incidence of CH in summer (11). Regarding the actual incidence of the disorder in newborns, before the start of screening programs in different countries, it was consistently underestimated due to lack of diagnosis so that it was reported to range from approximately 1 to 7000 per 10 000 live births. Following the implementation of the screening programs in developed countries, more accurate data on its incidence rate were estimated (2). According to evidence, the global incidence rate of the disorder varies from 14.7 per 1000 (1:67) infants in Nigeria to 0.14 per 1000 (1:7000) infants in Japan. Similarly, it has a varied incidence rate in the provinces of Iran (5,6), since the studies in Isfahan, Yazd, Mazandaran, southern Kerman and Shiraz have estimated the incidence rate of CH to be 1 per 370, 256, 2272, 137 and 1433 live births, respectively (3,5,6,14). However, the incidence rate of the disorder is higher in Iran than in industrialized countries; while it has been reported to vary from one per 370 to one per 1000 live births (2), averaging one per 670 live births (11)

Neonatal CH screening is one of the cost-effective preventive programs (6,7) and in the last 40 years. This screening has been able to considerably prevent the incidence of mental retardations and to reduce the resulting socioeconomic burden (6). In the pilot phase of the program in Iran, the cost-benefit ratio of the program was calculated to be approximately one to 14. However, after the implementation of the program, the ratio was calculated at one to 22, which shows that the program has been very fruitful in the country due to the high prevalence of CH in infants (11). National screening programs for CH in developed countries are aimed at facilitating early diagnosis and treatment of the disease and preventing its irreversible consequences, namely short stature and mental retardation (15). The high incidence rate of CH in Iran and its serious complications in case of late diagnosis, accentuate that the healthcare system of the country should be especially sensitive about its early diagnosis (8).

Objectives

The aim of this study was to investigate the incidence rate of CH in live neonates born in Chaharmahal and Bakhtiari province from 2015 to 2021 to help plan for the detection, identification, control, and treatment of CH at birth. As well, certain measures could be taken to prevent CH at different (first, second and third) levels.

Patients and Methods

Study design

The data of this study were obtained by the CH screening program from 2015 to 2021 (seven years) in the health deputy of Chaharmahal and Bakhtiari province. The screening program in the province has been officially implemented since the beginning of 2005 and sampling of infants at 3-5 days of age is currently being conducted in all urban and rural health centers. In the screening, all infants at the age of 3-5 days (golden time of screening) are referred to the screening unit of their place of residence and a blood sample is taken from their heel on a special filter paper approved by the ministry of health. The test were conducted on a daily basis in the provincial capital screening laboratory where the thyroid stimulating hormone (TSH) level of the blood sample is measured and the results were sent to the health deputy and also to the affiliated health centers. If the TSH level of the blood is 5-9.9 mU/L, re-sampling will be requested. Neonates with TSH levels of > 10 mU/L are referred for intravenous T4 and TSH tests and clinical examinations for confirmation of diagnosis. Infants with TSH levels of > 10 mU/L in the second stage (recall) and T4 levels of < 6.5 µg/dL are referred to a focal point physician. Finally, the infants diagnosed with CH are treated with levothyroxine and then, at the age of 3-5 years, TSH levels are measured to determine the type of CH for discontinuation the drug. Since in the case of transient type, there is no need to continue levothyroxine treatment (16,17).

Some infants, such as premature, twins or multiples, infants weighing less than 2500 g and over 4,000 g, those with hospitalization history, and those who have received a blood transfusion before sampling, may be tested 2 to 3 more times to prevent false-negative test results. False-negative test results refer to TSH levels of lower than the cut-off point during screening, which may be due to T4 deficiency or other thyroid problems especially in premature infants (18).

To conduct this study, the required information of all infants born between 2015 and 2021, living in the studied province and screened by referral laboratories was obtained from the deputy of health of the province and the non-communicable diseases unit.

Statistical analysis

The data was presented as frequency distribution and mean ± standard deviation.

Implication for health policy/practice/research/medical education

It can be claimed that Chaharmahal and Bakhtiari province, especially Lordegan, is one of the regions with high prevalence of congenital hypothyroidism in Iran, since the incidence rate is not only higher than the national average but also higher than the global average.

Results

From the beginning of 2015 to the end of 2021, a total of 128650 neonates, of which 67253 (52.27%) were boys, were born in the province. Screening coverage was 99.61% based on the number of samples and births. Around 88.24% of the samples were taken at the age of 3-5 days, 11.28 at the age of 6-21 days and only 0.48% of the samples

at the age over 22 days. TSH levels in 92.57%, 6.98%, 0.35% and 0.1% of neonates were below 5 mU/L, 5 to 9.9 mU/L, 10 to 19.9 mU/L and over 20 mU/L, respectively. Re-sampling was performed for 20.68% of infants, and the most common reason for re-sampling was TSH levels of 5-9.9 mU/L followed by inappropriate sample, history of hospitalization, weight less than 2500 g, multiple birth, prematurity, weight over 4000 g, history of taking certain medications and blood transfusions.

About 71.27% of the infants started their treatment at the optimal time of starting treatment, i.e., before the age of 28 days, 16.75% at the acceptable time, i.e., 29 to 40 days of age, and 11.98% of the infants started their treatment at the unfavorable time, i.e., after the age of 41 days. Moreover, 71.12% of the cases with late beginning of treatment (after the age of 29 days) in the whole province were from Lordegan, accentuating the necessity of finding potential causes of this observation.

In total, 651 infants were diagnosed with CH during the studied seven years and the incidence rate was obtained 5.06 per 1000 births (1 per 198 live births) in the province. The highest incidence rate of the disorder was observed in 2016 and the lowest incidence rate in 2021. Lordegan had the highest incidence rate (8.1 per 1000 live births) and Kiar had the lowest (1.67 per 1000 live births) during the studied period; as well, the highest and lowest incidence rates in terms of season were observed in winter and summer, respectively. It should be noted that the cities of Ben and Saman were part of Shahrekord County before 2018, and therefore the statistics related to the screening program in these two cities were merged with data of Shahrekord (Figures 1 to 3, Table 1).

Discussion

The incidence rate of CH in this study was estimated by dividing the number of final diagnoses by the number of

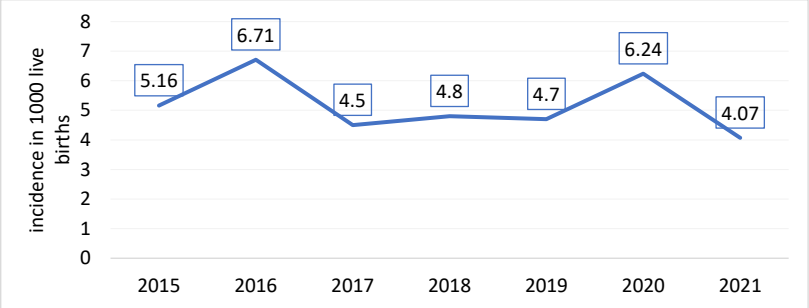

Figure 1. The trend of congenital hypothyroidism incidence from 2015 to 2021 by year.

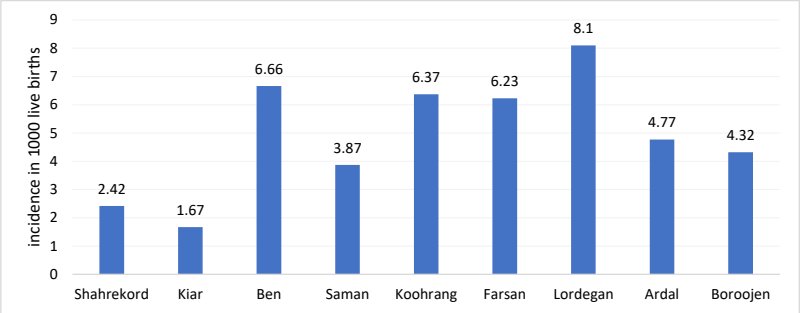

Figure 2. The average incidence of congenital hypothyroidism from 2015 to 2021 by city.

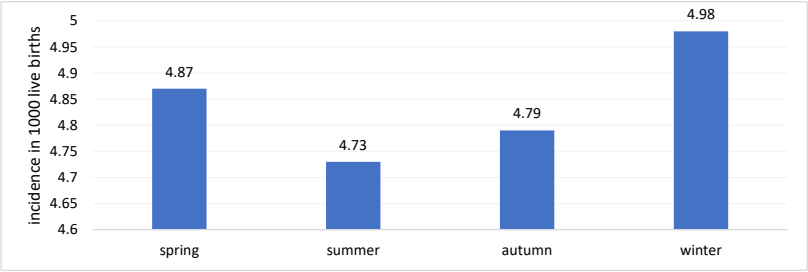

Figure 3. The average incidence of congenital hypothyroidism from 2015 to 2021 by season.

Table 1. Incidence of congenital hypothyroidism in the cities of Chaharmahal and Bakhtiari province by year

	2015	2016	2017	2018	2019	2020	2021	Total
Shahrekord	10	9	27	12	25	6	8	97
Kiar	3	0	0	3	1	2	1	10
Ben	0	0	0	4	0	5	4	13
Saman	0	0	0	1	3	2	2	8
Koohrang	4	4	6	7	8	6	2	37
Farsan	11	12	17	18	12	12	8	90
Lordegan	60	31	29	46	38	58	36	298
Ardal	8	8	3	7	4	2	4	36
Boroojen	6	9	9	9	6	16	7	62
Total	102	73	91	107	97	109	72	651

live births and calculated at one per 198 live births, which is higher than the national average and the rate reported from Shahrekord where the prevalence of the disorder from 2006 to 2014 was calculated at 111 per 54 468 live births (19). The study of Nele and Ghotbi in Kurdistan province, west Iran showed that the coverage of the screening program was 97% and the incidence rate of CH was 1 per 414 births (17). In a study conducted in China by Yao et al, a total of 91 921 334 infants were examined from 2013 to 2018 and 42 861 cases (4.66 per 10 000) of primary CH were identified (20). In a study by McGrath et al, in Ireland, among 2 361 174 infants examined between July 1979 and December 2016, 1063 (including 662 girls) developed CH (incidence rate: 0.45 per 1000 live births). The number of infants diagnosed with CH increased from 0.27 per 1000 live births treated between 1979 and 1991 to 0.41 per 1000 live births treated between 1992 and 2004. The corresponding statistic also increased to 0.65 per 1000 live births between 2005 and 2016 (21). In the study of Khanjani et al, the role of season and climate in the incidence of CH in Kerman province was investigated. The data were collected from CH screening program files from 2005 to 2011 in Kerman province, and 288,437 neonates were studied. Weather information was collected from the Meteorological Organization. The incidence rate of CH in Kerman province was 2.68 per 1000 live births and the monthly and seasonal incidence of CH was found to be significantly different (22).

Treatment in this province in 71.17% of cases was started in the golden time of treatment, i.e. before the age of 28 days, which is less than expected national index of treatment beginning (80%). The re-screening index due to inappropriate sample must be the least frequent reason according to national guidelines, while in our study re-screening due to inappropriate sample was drawn as the second reason, showing that further monitoring of the program implementation in this province is necessary.

One of the sensible explanations of the high incidence rate of transient CH is a lack of iodine or excess iodine in the mother's body, both of which are nutrition-related. Therefore, the salt iodization legislation was enacted in 1994 by the World Health Organization; and control of commercially available salts is one of the duties of the ministry of health in all provinces of Iran (18).

Conclusion

Taken together, it can be argued it can be argued that Chaharmahal and Bakhtiari province especially Lordegan is one of the regions with high incidence of CH in Iran, therefore the incidence rate is not only higher than the global average but also higher than the national average; thereby, the potential causes of this observation deserve further investigation. Besides this, better care and planning should be taken in the screening process to identify the issues related to this program and the main causes of the high incidence of the disease in this province, and to eliminate them as much as possible.

Limitations of the study

Because the data of this study were obtained from a provincial health deputy, we could not rely on its findings to arrive at a conclusive argument regarding the causes of CH, not to mention inconsistencies in available evidence.

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Authors' contribution

Conceptualization: MSM, YK and MMDB; Methodology: MSM, YK & RI; Validation: MSM and SP; Formal Analysis: YK and MMDB; Investigation: YK and MSM; Resources: SP and MMDB; Data Curation: MSM and YK; Writing—Original Draft Preparation: YK & MSM; Writing—Review and Editing: MSM, YK, MMDB, RI and SP; Visualization: MSM; Supervision: MSM; Project Administration: MSM; Funding Acquisition: MSM.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Shahrekord University of Medical Sciences approved this study (ethical No. IR.SKUMS.REC.1400.023). Written consent was taken from parents of participants.

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No.

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