Journal of Shahrekord University of Medical Sciences
doi: 10.34172/jsums.900 2025;27(2):55-59 http://j.skums.ac.ir

Original Article

# Etiological evaluation of congenital hypothyroidism in children over three years old in Chaharmahal and Bakhtiari province, Iran

**Noushin Rostampour[1], Majid Hamidi[2*], Abdolmajid Taheri[3], Mina Taslimi[4], Soleiman Kheiri[5]**

[1]Metabolic Liver Disease Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Department of Pediatrics, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
[3]Department of Radiology, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
[4]Student Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran
[5]Modelling in Health Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran

***Corresponding Author:** Majid Hamidi, Email: majid_hamidi48@yahoo.com

**Abstract**

**Background and aims:** The etiology of congenital hypothyroidism (CH) is important in determining its severity, prognosis, genetic counseling, and clinical management. The present study was performed to investigate the etiology of CH in children in Chaharmahal and Bakhtiari.

**Methods:** Screened children over the age of 3 years for hypothyroidism in the province were enrolled in this cross-sectional study. Then, in the case of permanent CH in the patient, demographic and laboratory findings, including thyroid-stimulating hormone (TSH) in primary screening, primary serum TSH, TSH after discontinuation of treatment, and age at the start of medication, were investigated, and patients were radiologically examined. The data were analyzed by SPSS 18 using descriptive statistics, a one-sample t-test, and a Chi-square test.

**Results:** Dyshormonogenesis accounted for the most etiological percentage of the disease (72%), followed by dysgenesis (28%). Gender was significantly associated with etiology ($P=0.022$). Thus, dyshormonogenesis was more common in boys. The weight ($P=0.564$) and length at birth ($P=0.978$), maternal age ($P=0.306$), age at the beginning of medication ($P=0.185$), primary filter TSH ($P=0.267$), primary serum TSH ($P=0.344$), and TSH after discontinuation of medication ($P=0.371$) were not significantly associated with etiological factors.

**Conclusion:** Among the etiological factors of CH, dyshormonogenesis was the most common cause among children in Chaharmahal and Bakhtiari province.

**Keywords:** Congenital hypothyroidism, Thyroxine hormone, Thyroid-stimulating hormone children

**Received:** July 10, 2023, **Accepted:** November 7, 2023, **ePublished:** June 29, 2025

## Introduction

Congenital hypothyroidism (CH) is caused by a deficiency of the thyroxine hormone (TH) in the fetus, infant, and breastfeeding babies for a variety of reasons (1). This disease is one of the most common problems that is currently of great importance and is widespread in different parts of Iran compared to the other regions of the world (2-4). It also imposes stupendous costs on the healthcare system (5,6). Due to the important role of thyroxine in neurological and skeletal growth, the limited time of this growth in early life, and even a short period of TH deficiency, can cause irreversible brain damage, eye misalignment, learning delay, short stature, and developmental problems in patients (7,8). One of the challenges in diagnosing and treating this disease is being asymptomatic, and as a result, its symptoms appear when its destructive effects on the body are stable (9). Therefore, screening is performed along with early diagnosis and treatment to identify the disease and control the treatment of affected infants at birth (10). Thus, early and prompt diagnosis and treatment of the disease (preferably in the first 2 weeks of life) play an important role in reducing or stopping the effects of CH (11). Birth weight, race, gender, age, the genetic affinity of parents, parental education, birth order, twin, type of delivery, and medication during pregnancy are considered risk factors for this disease (12,13).

On the other hand, CH has different etiologies and other causes that vary in different parts of the world and vary in Iran, depending on the different races of the Iranian people in different provinces.

According to the above-mentioned explanations and given the importance of diagnosing the etiology of the disease to decide on the treatment strategy-pathogenesis of the disease and providing prevention strategies and epidemiological studies (14), the present study seeks to determine the etiology of CH in children in Chaharmahal and Bakhtiari province.

## Materials and Methods

The present cross-sectional study was performed on children with CH in Chaharmahal and Bakhtiari province between 2017 and 2018. Samples were selected by convenience sampling and included all children at least 3 years old with permanent CH who were identified at birth screening. In addition, parental consent to participate in the study was considered an inclusion criterion.

Children who had normal thyroid-stimulating hormone (TSH) test results despite discontinued medication, patients who had no complete laboratory data, and patients who did not satisfactorily cooperate with radiological examination were excluded from the investigation. After coordination with the Health Department, children over 3 years of age who were diagnosed with CH were identified and selected in Chaharmahal and Bakhtiari province. Then, it was attempted to call their parents to evaluate their children's medical records.

The etiology of the disease was determined based on laboratory and radiological findings; ultrasound was performed for all patients to investigate the presence or absence of thyroid, and if thyroid tissue was not detected, patients were referred for a thyroid nuclear scan (15,16). Moreover, the ultrasound was conducted by a skilled sonographer. Among patients with CH, permanent type, length and weight at birth, maternal age, gender, maturity at birth, consanguinity, and history of thyroid disease in the parents were investigated and recorded in a checklist designed for this purpose.

Ultrasound and laboratory findings, including primary screening TSH, primary serum TSH, age at medication initiation, and TSH, were also identified and recorded after discontinuation of treatment, and their association with the obtained etiologies in patients underwent investigation.

The acquired data were analyzed by SPSS (version 18) using descriptive statistics (frequencies and percentages), a one-sample t-test, and a chi-square test.

## Results

A total of 100 children over the age of 3 with CH were included in the study, of whom 8 were normal in primary screening and were diagnosed with hypothyroidism after the development of hypothyroidism symptoms and performing additional tests. The age range of children was 3–14 years, with a mean ± standard deviation of 5.8 ± 2.45. The characteristics of the studied children are provided in Table 1.

The etiology was dyshormonogenesis in 72% of patients but dysgenesis in 28% of them. In the ultrasound of 5 patients, no thyroid tissue was found for whom a thyroid nuclear scan was asked to confirm the diagnosis. According to the results, tongue ectopic thyroid and atrophic thyroid were observed in 2 and 3 children, respectively (Table 2).

Tables 3 and 4 present data on the etiology (dyshormonogenesis and dysgenesis) obtained with other studied variables. According to the significance levels, only gender was associated with etiology, so the percentage of dyshormonogenesis was higher in boys than in girls (Table 3).

**Table 1.** Characteristics of patients with congenital hypothyroidism

| Variables | |
|---|---|
| Weight at birth (g), Mean ± SD | 2971 ± 556 |
| Length at birth (cm), Mean ± SD | 49.33 ± 2.75 |
| Maternal age (year), Mean ± SD | 12.27 ± 5.42 |
| Age at medication initiation (day), Mean ± SD | 25 ± 25.1 |
| Gender (female/male), No. (%) | 54.46 (54.46) |
| Premature, No. (%) | 14 (14) |
| Twin, No. (%) | 3 (3) |
| Consanguinity, No. (%) | 40 (40) |
| Paternal history of thyroid disease, No. (%) | 6 (6) |
| Maternal history of thyroid disease, No. (%) | 19 (19) |

*Note*. SD: Standard deviation.

None of the variables, such as the weight ($P = 0.564$) and length at birth ($P = 0.978$), maternal age ($P = 0.306$), age at the beginning of medication ($P = 0.185$), primary filter TSH ($P = 0.267$), primary serum TSH ($P = 0.344$), and TSH after discontinuation of medication ($P = 0.371$), were significantly related to etiological factors (Table 4).

## Discussion

The present study investigated the etiology of CH in children in the Chaharmahal and Bakhtiari province. According to the results, in 100 children with permanent CH from this province, dyshormonogenesis (72%) was the main cause of the disease, followed by dysgenesis (28%). In this regard, the results of a study in Isfahan province revealed that 72.3% of cases were due to thyroid dyshormonogenesis, while 27.7% of them were because of dysgenesis (17), which conforms to the results of the present study. In another study conducted by Karamizadeh et al, the rate of dyshormonogenesis was 57% compared to 43% obtained for dysgenesis (18), which is in agreement with the findings of the present study.

Another study in Iran showed that in cases with permanent CH, 68.2% had dyshormonogenesis, while 31.52% had thyroid dysgenesis (19). The findings of a study by Sun et al in China demonstrated that most cases of CH were due to thyroid dyshormonogenesis, and dysgenesis was the weaker cause of the disorder (20).

However, in a study performed in New Zealand, 67% of patients with CH were diagnosed with dysgenesis, and 33% had thyroid disease due to thyroid dyshormonogenesis (21).

In another study conducted in Alabama, USA, 23% of cases of permanent CH were related to thyroid dyshormonogenesis (22). This inconsistency in the results of studies can be due to differences in race and genetic factors that affect the etiology of the disease as an independent factor (22-24). Another study reported that demographic variables, especially ethnicity and age, affect the TSH level of the newborn (25). In the present

study, only gender was associated with etiology. More precisely, the percentage of dyshormonogenesis in boys was higher than that in girls. In this regard, some studies have shown that boys are at higher risk for neonatal hypothyroidism (26,27). However, in Saudi Arabia and China, the ratio of girls to boys with CH is 1.8 to 1 and 3 to 2, respectively (28,29).

However, in some studies, this ratio varied depending on the etiology of the disease. In another study, the ratio of females to males for the dyshormonogenesis cause was 105 to 128, but in the study of the causes of dysgenesis, the corresponding ratio was 65 to 53, respectively (17).

Numerous individual and environmental factors can explain the inconsistencies in the research findings. Rezaeian et al concluded that the birth season may act as an interactive factor that can increase the risk of CH in girls (30).

**Table 2.** Ultrasound status and thyroid nuclear scan of children with congenital hypothyroidism

| Variables | | Number of Patients | Percent |
|---|---|---|---|
| Thyroid ultrasound | Normal | 72 | 72 |
| | Hypoplasia | 23 | 23 |
| | Atrophy | 3 | 3 |
| | Ectopic | 2 | 2 |
| Etiological factors | Dyshormonogenesis | 72 | 72 |
| | Dysgenesis | 28 | 28 |

The results of this study revealed that none of the variables, including weight and length at birth, maternal age, age at the beginning of medication, primary filter TSH, primary serum TSH, TSH after medication discontinuation, maturity, and the relationship between parents and their medical history, were significantly associated with etiological causes of CH ($P > 0.05$).

In this respect, Bezen et al indicated that among the risk factors and laboratory findings, such as primary serum TSH, a significant relationship was found only between gender and permanent and transient CH (31).

A study in Iran showed that among the demographic characteristics, only family history was considered an etiological factor, and factors such as child development indicators and gender were not related to the etiology of the disease (19).

However, in a systematic review of the risk factors for CH, the reported risk factors for permanent CH with thyroid disorders included female gender, birth at high-risk geographical areas, family history of CH, maternal advanced age, and ethnicity. Risk factors identified for permanent CH with dyshormonogenesis were a family history of CH and the residence of both parents in high-risk areas (27). Moreover, although no association was found between primary TSH filter, primary serum TSH, TSH after medication discontinuation, and CH etiological causes in the present study, permanent CH was more pronouncedly associated with primary TSH levels than

**Table 3.** Frequency of etiology with qualitative variables

| Variable | Group level | Dyshormonogenesis | Dysgenesis | *P* Value[a] |
|---|---|---|---|---|
| | | Number (%) | Number (%) | |
| Gender | Male | 44 (81.5) | 10 (18.5) | 0.022* |
| | Female | 28 (60.9) | 18 (39.1) | |
| Maturity | Premature | 13 (92.9) | 1 (7.1) | 0.105 |
| | Mature | 59 (68.6) | 27 (31.4) | |
| Consanguinity | Yes | 29 (72.5) | 11 (27.5) | 0.928 |
| | No | 43 (71.7) | 17 (28.3) | |
| Paternal history of thyroid disease | Yes | 6 (100.0) | 0 (0.0) | 0.181 |
| | No | 66 (70.2) | 28 (29.8) | |
| Maternal history of thyroid disease | Yes | 15 (87.9) | 4 (21.4) | 0.454 |
| | No | 57 (70.4) | 24 (29.6) | |

*Significant ($P < 0.05$); [a] Chi-square test.

**Table 4.** Comparison of Quantitative Variables in Dyshormonogenesis and Dysgenesis Groups

| Group variable | Dyshormonogenesis | Dysgenesis | *P* value[a] |
|---|---|---|---|
| | Median (interquartile range) | Median (interquartile range) | |
| Weight at birth (g) | 3000 (2600-3395) | 3100 (2712-3375) | 0.564 |
| Length at birth (cm) | 50 (48-51) | 50 (48-50.75) | 0.978 |
| Maternal age (year) | 27 (23-30) | 28 (23.25-31) | 0.306 |
| Age at medication initiation (day) | 19.50 (13-30) | 16.5 (12-21.5) | 0.185 |
| Primary filter TSH level (mIU/L) | 9.5 (6.96-14.75) | 12.50 (7.12-33.40) | 0.267 |
| Primary serum TSH (mIU/L) level | 20.68 (15.78-47.70) | 33 (15.02-61.14) | 0.344 |
| TSH level (mIU/L) following medication discontinuation | 14.50 (10.83-21.80) | 18.22 (11.06-37.39) | 0.371 |

*Note*. TSH: Thyroid-stimulating hormone. [a] One-sample t-test.

transient hypothyroidism in the study of Karamizadeh et al (18).

The findings of another study in Egypt confirmed that primary TSH levels were higher in permanent CH cases than in transient cases, and other factors, such as growth and gender, were not linked to etiological factors (32).

## Conclusion

The results revealed that dyshormonogenesis is a common cause of permanent CH in Chaharmahal and Bakhtiari province. Moreover, dyshormonogenesis was higher in boys than in girls. Our findings can provide basic information to determine the therapeutic strategies and pathogenesis of CH in this province.

### Acknowledgments

This article was derived from a research project approved by the Research and Technology Deputy of Shahrekord University of Medical Sciences. Hereby, the researchers gratefully thank the patients who participated in this study.

### Authors' Contribution

**Conceptualization:** Noushin Rostampour.
**Data curation:** Majid Hamidi.
**Formal analysis:** Soleiman Kheiri .
**Funding acquisition:** Noushin Rostampour.
**Investigation:** Noushin Rostampour, Mina Taslimi.
**Methodology:** Noushin Rostampour, Abdolmajid Taheri.
**Project administration:** Majid Hamidi.
**Supervision:** Noushin Rostampour.
**Validation:** Majid Hamidi.
**Visualization:** Majid Hamidi.
**Writing–original draft:** Noushin Rostampour, Majid Hamidi.
**Writing–review & editing:** Noushin Rostampour, Majid Hamidi.

### Competing Interests

The authors declare that there is no conflict of interests.

### Ethical Approval

This study protocol was approved by the Ethics Committee of Shahrekord University of Medical Sciences (IR.SKUMS.REC.1396.182).

### Funding

This study was financially supported by Shahrekord University of Medical Sciences, Iran.

### References

1. Uthayaseelan K, Kadari M, Subhan M, Saji Parel N, Krishna PV, Gupta A, et al. Congenital anomalies in infant with congenital hypothyroidism: a review of pathogenesis, diagnostic options, and management protocols. Cureus. 2022;14(5):e24669. doi: 10.7759/cureus.24669.
2. Doustmohamadian S, Mehrizi S, Rahbar MN, Mirmohammadkhani M. Congenital hypothyroidism and its related factors in an Iranian population: a retrospective study in Semnan (2011-2016). Int J Prev Med. 2020;11:169. doi: 10.4103/ijpvm.IJPVM_254_19.
3. Beheshti Z, Rezaei R, Alipour A, Kosarian M, Saatsaz S. A 7-year study on the prevalence of congenital hypothyroidism in northern Iran. Electron Physician. 2018;10(4):6689-96. doi: 10.19082/6689.
4. Aminzadeh M. Higher prevalence of permanent congenital hypothyroidism in the southwest of Iran mostly caused by dyshormonogenesis: a five-year follow-up study. Arch Endocrinol Metab. 2018;62(6):602-8. doi: 10.20945/2359-3997000000085.
5. Vidavalur R. Human and economic cost of disease burden due to congenital hypothyroidism in India: too little, but not too late. Front Pediatr. 2022;10:788589. doi: 10.3389/fped.2022.788589 .
6. Karunarathna N, Hettiarachchi M. Cost-Effective Analysis of the Congenital Hypothyroidism Screening Program in Sri Lanka. Value Health Reg Issues. 2021;24:181-6. doi: 10.1016/j.vhri.2021.01.001.
7. Bernal J. Thyroid hormones in brain development and function. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, et al, eds. Endotext [Internet]. South Dartmouth, MA: MDText.com, Inc.; 2000. Available from: https://www.ncbi.nlm.nih.gov/books/NBK285549/. Updated January 14, 2022.
8. Liu YY, Brent GA. Thyroid hormone and the brain: mechanisms of action in development and role in protection and promotion of recovery after brain injury. Pharmacol Ther. 2018;186:176-85. doi: 10.1016/j.pharmthera.2018.01.007.
9. Bauer AJ, Wassner AJ. Thyroid hormone therapy in congenital hypothyroidism and pediatric hypothyroidism. Endocrine. 2019;66(1):51-62. doi: 10.1007/s12020-019-02024-6.
10. Shaghaghian S, Rahimi N, Mousavi-Roknabadi RS, Azadian F, Nazemzadegan B, Ghasempour H, et al. Appropriateness of congenital hypothyroidism screening program in Fars province, Iran: a retrospective study from 2005 to 2015. Iran J Med Sci. 2019;44(3):245-50.
11. Leung AK, Leung AA. Evaluation and management of the child with hypothyroidism. World J Pediatr. 2019;15(2):124-34. doi: 10.1007/s12519-019-00230-w.
12. Zhou J, Luo J, Lin J, Zeng Y, Qiu X, Zhu W, et al. Perinatal risk factors for congenital hypothyroidism: a retrospective cohort study performed at a tertiary hospital in China. Medicine (Baltimore). 2020;99(26):e20838. doi: 10.1097/md.0000000000020838.
13. Bowden SA, Goldis M. Congenital Hypothyroidism. [Updated 2023 Jun 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK558913/
14. Hemati Z, Hashemipour M, Hovsepian S, Mansourian M, Zandieh M, Ahmadian M, et al. Congenital hypothyroidism in different cities of the Isfahan province: a descriptive retrospective study. J Educ Health Promot. 2019;8:137. doi: 10.4103/jehp.jehp_219_18.
15. Chun S, Lee YS, Yu J. Thyroid imaging study in children with suspected thyroid dysgenesis. Ann Pediatr Endocrinol Metab. 2021;26(1):53-9. doi: 10.6065/apem.2040120.060.
16. Chaudhary V, Bano S. Thyroid ultrasound. Indian J Endocrinol Metab. 2013;17(2):219-27. doi: 10.4103/2230-8210.109667.
17. Hashemipour M, Ghasemi M, Hovsepian S, Heiydari K, Sajadi A, Hadian R, et al. Etiology of congenital hypothyroidism in Isfahan: does it different? Adv Biomed Res. 2014;3:21. doi: 10.4103/2277-9175.124658.
18. Karamizadeh Z, Dalili S, Sanei-Far H, Karamifard H, Mohammadi H, Amirhakimi G. Does congenital hypothyroidism have different etiologies in iran? Iran J Pediatr. 2011;21(2):188-92.
19. Dalili S, Rezvani SM, Dalili H, Mohtasham Amiri Z, Mohammadi H, Abrisham Kesh S, et al. Congenital hypothyroidism: etiology and growth-development outcome. Acta Med Iran. 2014;52(10):752-6.
20. Sun F, Zhang JX, Yang CY, Gao GQ, Zhu WB, Han B, et al. The genetic characteristics of congenital hypothyroidism in China by comprehensive screening of 21 candidate genes. Eur J Endocrinol. 2018;178(6):623-33. doi: 10.1530/eje-17-1017.
21. Albert BB, Cutfield WS, Webster D, Carll J, Derraik JG, Jefferies C, et al. Etiology of increasing incidence of congenital hypothyroidism in New Zealand from 1993-2010.

J Clin Endocrinol Metab. 2012;97(9):3155-60. doi: 10.1210/jc.2012-1562.
22. Pitts L, McCormick W, Mick GJ. Congenital hypothyroidism: 8-year experience using 2 newborn screens in Alabama. Horm Res Paediatr. 2019;91(5):319-28. doi: 10.1159/000501395.
23. Kwak MJ. Clinical genetics of defects in thyroid hormone synthesis. Ann Pediatr Endocrinol Metab. 2018;23(4):169-75. doi: 10.6065/apem.2018.23.4.169.
24. Grasberger H, Refetoff S. Genetic causes of congenital hypothyroidism due to dyshormonogenesis. Curr Opin Pediatr. 2011;23(4):421-8. doi: 10.1097/MOP.0b013e32834726a4.
25. Heather NL, Derraik JG, Webster D, Hofman PL. The impact of demographic factors on newborn TSH levels and congenital hypothyroidism screening. Clin Endocrinol (Oxf). 2019;91(3):456-63. doi: 10.1111/cen.14044.
26. Esmailnasab N, Moasses Ghaffari B, Afkhamzadeh A. Investigation of the risk factors for congenital hypothyroidism in the newborns in Kurdistan Province. Sci J Kurdistan Univ Med Sci. 2012;17(4):103-8. [Persian].
27. Hashemipour M, Samei P, Kelishadi R, Hovsepian S, Hani Tabaei Zavareh N. A systematic review on the risk factors of congenital hypothyroidism. J Pediatr Rev. 2019;7(4):199-210. doi: 10.32598/jpr.7.4.199.
28. Al-Jurayyan NA, Shaheen FI, Al-Nuaim AA, El-Desouki MI, Faiz A, al Herbish AS, et al. Congenital hypothyroidism: increased incidence in Najran province, Saudi Arabia. J Trop Pediatr. 1996;42(6):348-51. doi: 10.1093/tropej/42.6.348.
29. Zhang YQ, Cao QX. Experience in neonatal screening for congenital hypothyroidism. Chin Med J. 1993;106(3):216-9. doi: 10.5555/cmj.0366-6999.106.03.p216.01.
30. Rezaeian S, Moghimbeigi A, Esmailnasab N. Gender differences in risk factors of congenital hypothyroidism: an interaction hypothesis examination. Int J Endocrinol Metab. 2014;12(2):e13946. doi: 10.5812/ijem.13946.
31. Bezen D, Dilek E, Torun N, Tütüncüler F. Etiological evaluation of primary congenital hypothyroidism cases. Turk Pediatri Ars. 2017;52(2):85-91. doi: 10.5152/TurkPediatriArs.2017.3989.
32. Bekhit OE, Yousef RM. Permanent and transient congenital hypothyroidism in Fayoum, Egypt: a descriptive retrospective study. PLoS One. 2013;8(6):e68048. doi: 10.1371/journal.pone.0068048.