OPEN ACCESS

ISSN: 2676-7473

RBMS.2020; 25(1):e14

ORIGINAL RESEARCH

Comparison of growth indices between patients with treated congenital hypothyroidism and healthy children in the Kurdish population: a historical cohort study

Behnam Arabzadeh[*1], Nazanin Hajizadeh[2]

1. *Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
2. *Preventative Gynecology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

*Corresponding Author:
Address: Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Email: behnamarabzade2000@gmail.com

Date Received: May 2020 *Date Accepted: June 2020* *Online Publication: August 15, 2020*

Abstract

Objective: Congenital hypothyroidism (CH) refers to a condition in which there is a low level of thyroid hormone in an infant's blood. It can result in serious problems in physical and mental development of patients. This study aimed to compare growth indices in patients with and without CH.

Materials and Methods: Historical cohort study, 96 patients with CH in different counties of Kurdistan province were considered as exposed cases. The non-exposed group included children of the same age, sex and geographical area as much as possible. Independent t-test was used to compare growth indices in the two groups. Moreover, repeated measurement was used to compare the two groups in terms of trend of changes in growth.

Results: There was a significant difference between the two groups of neonates in terms of weight and head circumference measured at third and ninth months of ages ($p<0.05$) respectively. Moreover, no statistically significant difference was observed between the two groups in terms of the trend of changes in growth percentiles (head circumference, height, and weight) ($p>0.05$).

Conclusion: The quality of care provided for CH patients in Kurdistan province is at a desirable level.

Keywords: Growth indices, Congenital hypothyroidism, Historical cohort, Iran

Introduction

Congenital hypothyroidism (CH) is one of the most common diseases of endocrine metabolism and one of the most frequent causes of treatable physical growth disorders and mental disability (1). Patients with congenital hypothyroidism have low levels of thyroid hormone in their blood; such a condition is due to defects in the structure of the thyroid gland, defects in biosynthesis of thyroid hormone, or malfunction of hypothalamus or Pituitary gland (2).

Most neonate with CH are normal at birth, but in the event of late diagnosis and treatment, impaired physical and neurological development of the impulse, such as mental retardation (3, 4). Timely and effective treatment, achieving a good metabolic control, and maintaining these conditions during treatment can help to maintain normal intelligence quotient and ensure normal growth and development of the patient. Different studies have shown varies finding from the growth of neonate with CH. It seems that there are several factors, including starting time ,initial dose, disease severity ,affect to physical normality of neonate (4).The incidence of CH varies in different regions. The disease incidence has been reported 1:800-3000 live births in the world (5-8), In Iran, several studies indicate different incidence of CH (9-11). In Kurdistan Province, a western province in Iran which is located in a mountainous region, the population is mainly from Kurd ethnicity and the prevalence of the disease is about one per 414 live births (12).

Of the total patients 202 (22.6%) were permanent and The mean start of treatment was 21 days after birth (13). Another study evaluated the neurocognitive impairments in CH Patients have been done in Kurdistan province (14), therefore in this study; we decided to comparison the anthropometric indices of children with CH with healthy infants.

Materials and Methods

This study was a retrospective (historical) cohort study that was conducted in 2014 in Kurdistan province located in west of Iran. The study was approved by the ethics committee of Kurdistan University of Medical Sciences. After selecting the subjects, their parents were contacted and the objectives of the study were explained; then, the parents were asked to allow home visits. Before visiting homes of the subjects, their medical files were reviewed and the required data were recorded so that to find the deficiencies.

A total of 96 children with congenital hypothyroidism aged more than 42 months, who were diagnosed in different counties of Kurdistan during the years 2005-2013, were considered as exposed group and enrolled into the study via census sampling method. Congenital hypothyroidism screening program was started in Iran in 2005. This program collects patient data from every county; the forms used in this program are the same all across the country and they are completed on a regular basis. In order to implement congenital hypothyroidism screening program, three to five days after birth a Lancet was used to collect a few drops of blood from the baby's heel. The blood drops were poured on a paper filter. After drying, which usually took three hours, using priority mail they were sent to neonatal screening laboratories in the capital city of the province. After conducting the tests, the cases with a TSH less than 5 mu/L were classified as healthy children and the other cases which were susceptible were invited for further tests. In patients with a THS between 5 and 9.9, the second paper filter was obtained and those with a TSH more than 10 were referred to a focal point to undergo serum tests for confirmation or rejection of the disease. The ideal time for starting treatment is about two to three weeks after birth. The exposed infants were treated with a dose of 10 to 15 μg/kg/day of levothyroxine. Monitoring of TSH and T4 was done every 1-2 month during the first year of life and every 1-3 month during the second and third year. After three years of treatment of the disease, the process of treatment was stopped for two to four weeks and the tests were repeated to determine whether the disease is transient or permanent. The cases with normal test results were classified as transient cases and the treatments for them was discontinued, otherwise the patient was classified as a permanent type and the patients had to continue the treatment until the end of their life (15). The non-exposed group included children of the same age and sex who were selected from the same geographical area as much as possible. The results of their hypothyroidism screening test

were normal. The members of this group were selected using the list of vaccination registered in the studied health centers.

Eligibility for including in this study were cases had CH diagnosed by a newborn screening program and confirmed by venous blood samples, and also if they had been treated with levothyroxine, and CH patients with concomitant disease or complications such as genetic disorders, IUGR, prematurity were excluded.

Assessment tool: After selecting the subjects, their medical files were reviewed. Anthropometric data of the studied children were collected from their medical files, which had been already registered in the health centers. Supine length until the age of 2 years (before walking) and then standing height were measured without shoes by using a tape meter against a wall with a precision of 10mm. weight was measured with scale that was placed on a flat ground. Head circumference was measured using a non-elastic tape with a precision 0f 10 mm(16). The data on care services provided for the patients with congenital hypothyroidism were extracted either from files registered in physicians' offices (if the patient received medical care form a specialist), from the medical files registered in the health centers (if the patient received medical care from physicians working in health centers), or from their treatment cards which were registered by their parents.

The collected data were entered into SPSS version 20 software and mean and frequency of each item were calculated for each group. Independent t-test was used to compare growth indices in the two groups. In addition, Repeated Measurement test was used to compare the two groups in terms of the trend of growth. Chi-square test and Fisher's test were used to compare the qualitative indicators.

Results

Our study was conducted on a total of 192 persons, of whom 96 persons had congenital hypothyroidism and the other 96 persons were normal. Of all, 118 subjects (62%) were male and half of them (59 persons) had congenital hypothyroidism; moreover, 74 persons (38%) were female and half of them (37 persons) had congenital hypothyroidism. Of all, 72.6% were living in urban areas and 27.4% in rural areas. Based on the results, 97.8% of infants with congenital hypothyroidism and 100% of normal infants were breast-fed. The mean (SD) age of mothers at the time of delivery was 28.3 ± 5.4 years in those whose neonates had hypothyroidism and 29 ± 6.8 years in those with normal neonates.

There was no statistically significant difference between the two groups in terms of the number of children (p=0.533), mother's education (p=0.552), father's education (p=0.157), father's job (p=0.199), location of residence (p=1.000), type of milk used for feeding the child (p=0.497), mean age of mother at the time of childbirth (p=0.410).

As shown in Table 1, there was a statistically significant difference between the two groups in terms of the mean head circumference at ninth months of age (p=0.008).

Table 1: Comparison of the two studied groups in terms of mean head circumference and heightand weight

Variable		Head		Height		Weight	
Time Interval	N	Mean (SD)	P	Mean (SD)	P	Mean (SD)	P
At Birth			0.18		0.65		0.36
Normal	87	54.8 (27.9)		49.4 (25)		52 (27.6)	
Hypothyroidism	87	48.6 (32.1)		47.6 (25.6)		48 (30.9)	
3 Month			0.13		0.34		0.02
Normal	35	52.9 (25.1)		61.5 (24)		66.8 (22.1)	
Hypothyroidism	35	42.8 (30.1)		55.6 (27.9)		51.8 (32)	
6 Month			0.22		0.84		0.13
Normal	96	48.5 (23.3)		54.3 (23.7)		53.3 (25.1)	
Hypothyroidism	96	44 (26.7)		55 (24.8)		55 (24.8)	
9 Month			0.008		0.08		0.08
Normal	31	53.2 (27.8)		63 (23.6)		48.5 (27)	
Hypothyroidism	30	34.4 (25.2)		52.7 (20.7)		52.7 (20.7)	
12 Month			0.19		0.53		0.52
Normal	91	42.9 (24.8)		51 (25.3)		38.7 (25.5)	
Hypothyroidism	91	37.9 (26.3)		48.7 (25.1)		36.2 (27.5)	
18 Month			0.74		0.23		0.63
Normal	61	44 (24.7)		45.2 (22.7)		45.2 (22.7)	
Hypothyroidism	61	42.5 (28)		50.8 (28.3)		50.8 (28.3)	
24 Month			0.37		0.65		0.06
Normal	41	46 (24.8)		44.7 (23.7)		40 (23.5)	
Hypothyroidism	42	51.4 (29.6)		47.4 (30.3)		45 (26.6)	
30 Month			-		0.16		0.32
Normal	28	-		49.5 (24.4)		43 (20.9)	
Hypothyroidism	29	-		59.4 (28.4)		54.7 (25.9)	
36 Month			-		0.08		0.08
Normal	28	-		51.6 (25.7)		43.5 (25.7)	
Hypothyroidism	29	-		64.6 (29.4)		55.3 (27.9)	

The results of repeated measurement analysis showed no significant difference between the two groups in terms of the trend of changes in head circumference growth percentile. There was no statistically significant difference between the two groups in terms of the mean height of children from birth to 36th months of age (p>0.05). The results of Repeated Measurement analysis showed no significant difference between the two groups in terms of the trend of changes in height growth percentile. Also, there was a statistically

significant difference between the two groups in terms of the mean weight of children at third months of age (p=0.002). The results of Repeated Measurement analysis showed no significant difference between the two groups in terms of the trend of changes in weight growth percentile.

Discussion

This study used anthropometric indicators to evaluate the growth of children with congenital hypothyroidism; the patients had been already detected by a screening program and were under treatment. Based on the findings of this study, growth parameters in children with congenital hypothyroidism were different from those in the control group however with increasing the age of children in both groups, height, weight, and head circumference of patients got closer to those of normal children and the differences became trivial. In other words, timely and appropriate treatment of children with congenital hypothyroidism may help to grow up children with almost normal height, weight, and head circumference. In this study, there was a significant difference between the two groups in terms of mean head circumference of the subjects nine month after birth. Moreover, there was a difference between the two groups in terms of the mean weight of the subjects three months after birth however there was no difference between the two groups in terms of the mean height.

In a study conducted in Spain, there was no significant difference between patients with congenital hypothyroidism and normal group in terms of height and body mass index (BMI). However, three months after birth, there was a statistically significant difference between the two groups of children in terms of weight ($p < 0.02$) which is in line with the results of our study (17). On the other hand, in a study by Siragusa, head circumference of people who had been affected by neonatal congenital hypothyroidism was significantly more than that of the normal subjects(18). In Bucher's study it was found that one to three months after birth head circumference of children under levothyroxine treatment become similar to that of the normal subjects; moreover, with increasing age and continuing the course of treatment, patients' head circumference was significantly increased (19).

In a study conducted in France, height, weight, head circumference, and BMI of the subjects were measured and it was found that the mean height of children aged one and two years with severe congenital hypothyroidism was lower than the normal range; it might be attributed to the physical factors related to the height measurement and estimation methods (20). However, at the ages of three to four years, mean height of patients was normal that is consistent with our results.

In our study, Repeated Measurement analysis was used to compare the trends of changes in growth percentiles of head circumference, height, and weight; according to the results, no significant difference was observed between the two groups (Figure 1, 2, 3). However, in a study by Faizi et al., there were statistically significant differences between children with congenital hypothyroidism and normal subjects in terms of growth percentiles of weight, height, and head circumference ($p<0.001$)(4).

The results showed that timely diagnosis and appropriate treatment of newborns with congenital hypothyroidism led to improvements in growth percentiles (head circumference, height, weight) from birth up to 36^{th} month of age. Although some differences were observed at different time intervals, appropriate care services and treatment interventions were effective in reducing the differences between the two groups in terms of growth percentiles.

In order to further investigate the factors that contribute to differences in growth indices in children with congenital hypothyroidism (as compared with the normal population), it is suggested to carry out a prospective cohort study or conduct a nested case-control study to investigate multiple factors affecting congenital hypothyroidism. Low awareness of the families, health and medical personnel, and physicians can lead to delays in timely diagnosis and appropriate treatment of newborns with the disease; it can have irreversible effects on individuals, families, and the community. In order to appropriately manage treatment services it is necessary to make proper plans, involve families in the programs to pay more attention to the disease, and promote physicians' awareness about suitable disease control methods. In addition, regular monitoring and accurate measurement

of growth indices in normal infants and children with the disease can help to decrease the differences between normal population and the patients in terms of growth indices.

Acknowledgments
This study was the result of a research project, which was approved by the Research Deputy of Kurdistan University of Medical Sciences and has been conducted under their financial support. We would like to thank them for their special attention to this project.

Conflict of interest
The authors have no conflict of interest to declare.

References:

1. Fisher DA, Dussault JH, Foley TP, Klein AH, LaFranchi S, Larsen PR, et al. Screening for congenital hypothyroidism: results of screening one million North American infants. The Journal of pediatrics. 1979;94(5):700-5.
2. Jameson2. Jameson J, Anthony P, weetman .Disease of the thyroid gland.Harrison'sgland. Harrison's principles of internal medicine. 16th edEd. New York. MC Grow-Hill medical pub 2008; 10: 2104-8.
3. Unüvar T, Demir K, Abacı A, Büyükgebiz A, Böber E. The role of initial clinical and laboratory findings in infants with hyperthyrotropinemia to predict transient or permanent hypothyroidism. Journal of clinical research in pediatric endocrinology. 2013;5(3):170-3.
4. Feizi A, Hashemipour M, Hovsepian S, Amirkhani Z, Kelishadi R, Yazdi M, et al. Growth and specialized growth charts of children with congenital hypothyroidism detected by neonatal screening in isfahan, iran. ISRN endocrinology. 2013;2013.
5. Gaudino R, Garel C, Czernichow P, Léger J. Proportion of various types of thyroid disorders among newborns with congenital hypothyroidism and normally located gland: a regional cohort study. Clinical endocrinology. 2005;62(4):444-8.
6. Skordis N, Toumba M, Savva SC, Erakleous E, Topouzi M, Vogazianos M, et al. High prevalence of congenital hypothyroidism in the Greek Cypriot population: results of the neonatal screening program 1990-2000. Journal of Pediatric Endocrinology and Metabolism. 2005;18(5):453-62.
7. Harris KB, Pass KA. Increase in congenital hypothyroidism in New York State and in the United States. Molecular genetics and metabolism. 2007;91(3):268-77.
8. Desai MP. Disorders of thyroid gland in India. The Indian Journal of Pediatrics. 1997;64(1):11-20.
9. Hashemipour M, Amini M, Iranpour R, Sadri GH, Javaheri N, Haghighi S, et al. Prevalence of congenital hypothyroidism in Isfahan, Iran: results of a survey on 20,000 neonates. Hormone Research in Paediatrics. 2004;62(2):79-83.
10. Karamizadeh Z. Incidence of congenital hypothyroidism in Fars Province, Iran. Iran J Med Sci. 1992;17:78-80.
11. Ordookhani A, Mirmiran P, Moharamzadeh M, Hedayati M, Azizi F. A high prevalence of consanguineous and severe congenital hypothyroidism in an Iranian population. Journal of pediatric endocrinology and metabolism. 2004;17(9):1201-10.
12. NELE S, GHOTBI N. Congenital hypothyroidism screening program in Kurdistan, Iran. 2011.
13. Goodarzi E, Ghaderi E, Khazaei S, Alikhani A, Ghavi S, Mansori K, et al. The prevalence of transient and permanent congenital hypothyroidism in infants of Kurdistan Province, Iran (2006-2014). International Journal of Pediatrics. 2017;5(2):4309-18.
14. Nili S, Ghaderi E, Ghotbi N, Baneh FV. COMPARISON OF IQ BETWEEN PATIENTS WITH TREATED CONGENITAL HYPOTHYROIDISM AND HEALTHY CHILDREN IN THE KURDISH POPULATION-A HISTORICAL COHORT. Acta Endocrinologica (1841-0987). 2015;11(3).
15. Executive instruction of national newborn screening program for Congenital Hypothyroidism in Iran, Ministry of Health & Medical Education, 2013.
16. Fathei BB, Elahe, International Journal of Pediatrics. 2016;5(2):5684-18.
17. Gibert AA, Vicens-Calvet E, Carrascosa LA, Bargadá EM, Potau VN. [Growth and maturation in the patients with congenital hypothyroidism detected by the neonatal screening program in

Catalonia, Spain (1986-1997)]. Medicina clínica. 2010;134(7):287-95.
18. Siragusa V, Terenghi A, Rondanini G, Vigone M, Galli L, Weber G, et al. Congenital hypothyroidism: auxological retrospective study during the first six years of age. Journal of endocrinological investigation. 1996;19(4):224-9.
19. Bucher H, Prader A, Illig R. Head circumference, height, bone age and weight in 103 children with congenital hypothyroidism before and during thyroid hormone replacement. Helvetica paediatrica acta. 1985;40(4):305-16.
20. Grant D. Growth in early treated congenital hypothyroidism. Archives of disease in childhood. 1994;70(6):464-8.