IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

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Original Article

Prevalence of Sensorineural Hearing Loss in Patients with Congenital Hypothyroidism in Qazvin, Iran (2015)

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ABSTRACT

Background: Congenital hypothyroidism increases the risk of sensorineural hearing loss (SNHL). Children with hearing impairment are prone to communication disorders. The present study aimed to determine the prevalence of SNHL in patients with congenital hypothyroidism in Qazvin, Iran.

Methods: This cross-sectional study was conducted on children with transient or permanent congenital hypothyroidism in Qazvin province, Iran in 2015. The patients were identified through national neonatal thyroid screening during 2006-2011. Hearing loss was assessed using the auditory brainstem response (ABR). A minimum of three years of follow-up was carried out to determine the permanency of congenital hypothyroidism. Data analysis was performed using t-test and Chi-square.

***Results*:** In total, 155 children with congenital hypothyroidism were enrolled in the study, including 67 females (43.2%) and 151 cases of primary congenital hypothyroidism. Abnormal ABR was observed in 10 patients (6.45%) (6.6% in permanent cases and 6.1% in transient cases), seven of whom were female. In addition, eight patients with primary congenital hypothyroidism and two patients with central congenital hypothyroidism had abnormal ABR (P=0.165). Mean primary thyroid-stimulating hormone levels (52.45±39.91 versus 38.23±28.03 IU/l; P=0.355) and T4 (6.07±4.33 versus 6.98±3.40 µg/dl; P=0.307) had no significant differences in the children with SNHL and other patients. At the beginning of the treatment, mean age of the children with SNHL was 28.50±22.13 days, while it was 28.87±30.34 days in the other subjects (P=0.909).

Conclusion: According to the results, the prevalence of SNHL was lower in the patients with congenital hypothyroidism compared to the reported rates in other countries. However, the assessment of hearing loss should be prioritized in the infants with congenital hypothyroidism.

Keywords: Communication disorders, Congenital hypothyroidism, Diagnosis, Mass screening, Sensorineural hearing loss

Introduction

The prevalence of congenital hypothyroidism is one per 2,000-4,000 live births worldwide (1-3), while the incidence of congenital hypothyroidism is 2 per 1,000 live births in Iran (4-8). Congenital hypothyroidism is one of the most common treatable causes of mental retardation in infants (9-11).

Hypothyroidism is caused by reduced thyroid hormone synthesis or hormone receptor dysfunction. Hypothyroidism may be congenital or acquired. Most cases of congenital hypothyroidism are sporadic, and only 2% of the cases are reported to be familial. Congenital hypothyroidism has the female-to-male ratio of 2:1 (12). Insufficient disease control is considered to be the most significant contributing factor to the poor school performance of children with congenital hypothyroidism (13).

In several cases of congenital hypothyroidism, there is severe and permanent thyroid hormone

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Please cite this paper as:
Saffari F, Nikpendar MH, Esmailzadehha N, Oveisi S, Homaei A, Jalilolghadr Sh. Prevalence of Sensorineural Hearing Loss in Patients with Congenital Hypothyroidism in Qazvin, Iran (2015). Iranian Journal of Neonatology. 2018 Sep: 9(3). DOI: 10.22038/ijn.2018.26901.1356

deficiency, and the symptoms manifest since the first week of life. Reports suggest that 85% of the permanent cases are due to thyroid dysgenesis. In addition, some causes of transient congenital hypothyroidism are caused due to the maternal use of anti-thyroid drugs during pregnancy, maternal deficient/increased iodine intake, and hypothalamic-pituitary dysfunction (1). Transplacental passage of maternal thyroxin plays a key role in fetal brain development, inducing approximately 33% of normal thyroxin serum levels in neonates. Maternal hypothyroidism during pregnancy may lead to permanent defects in the fetal development process (14, 15).

Most of the neonates with congenital hypothyroidism (even with thyroid agenesis) are asymptomatic at birth. Therefore, neonatal screening is essential to the diagnosis of congenital hypothyroidism. The prevalence of congenital abnormalities is only 3% in the general population and 10% in the patients with congenital hypothyroidism (13, 16).

Congenital hypothyroidism increases the risk of sensorineural hearing loss (SNHL). According to animal studies, thyroid hormones play a pivotal role in the development of the internal auditory system. Furthermore, animal studies have denoted that the absence of thyroid hormones at the end of pregnancy and after birth could lead to untreatable hearing loss due to external hair cell dysfunction and potassium transfer in the inner ear (17).

The prevalence of SNHL in patients with congenital hypothyroidism is approximately 20% (12). Normal hearing is essential to the formation of lingual skills in children, and children with hearing impairment are prone to communication disorders (18). Reports have suggested the higher prevalence of congenital hypothyroidism in various regions in Iran compared to other countries, and limited research has been conducted in Qazvin province (Iran) in this regard.

The present study aimed to determine the prevalence of SNHL in patients with congenital hypothyroidism in Qazvin, Iran.

Methods

This cross-sectional study was conducted on the children with congenital hypothyroidism in Qazvin province, Iran in 2015. The study protocol was approved by the Ethics Committee of Qazvin University of Medical Sciences. Written informed consent was obtained from the parents of the neonates at the beginning of the study.

Inclusion criterion of the study was the diagnosis of congenital hypothyroidism (transient or permanent) in neonatal thyroid screening during 2006-2011 as confirmed by a pediatric endocrinologist. In thyroid screening, the levels of thyroid-stimulating hormone (TSH) and T4 were ≥10 U/l and <6.5 µg/dl, respectively 28 days after birth, which was considered as congenital hypothyroidism. A minimum of three years of follow-up was performed to determine the permanency of congenital hypothyroidism in the subjects. Permanent congenital hypothyroidism was defined as the need for thyroid hormone treatment after the age of three years (13).

A datasheet was provided including the demographic characteristics and medical and family history of the patients. In addition, the history of underlying diseases that may affect hearing was documented. Increased TSH level to more than 5 U/l during the treatment for ≥4 times after the age of six months was defined as insufficient control, and relative control was defined in the case of increased TSH levels less than four times (13).

Hearing loss was assessed using the auditory brainstem response (ABR) after the age of four months. ABR is a valid and sensitive method to evaluate auditory function in the peripheral nervous system and brainstem, which could be applied for screening and diagnosis purposes. Auditory stimulation begins with 30-40 decibel intensity, decreases gradually to the hearing threshold (15-20 db), and the responses are evaluated afterwards. In the presence of responses, the child has normal or near-normal hearing sensitivity within the frequency range of 1,000-4000 hertz. This level of hearing is sufficient for speaking and acquiring lingual skills. The absence of responses is an indicator of impaired sensorineural hearing (19).

Data were expressed as mean, standard deviation, frequency, and percentage. Categorical data were analyzed using Chi-square, and continuous variables were compared using t-test. In all the statistical analyses, P-value of less than 0.05 was considered significant.

Result

In total, 155 children with congenital hypothyroidism were enrolled in the study, and 67 patients (43.2%) were female. Parents of 23 patients had a familial first-cousin marriage, and parents of 10 patients (6.5%) had a familial second-cousin marriage. Among the subjects, 151 cases had primary congenital hypothyroidism, and four cases (2.58%) had central congenital

hypothyroidism. Mean age at diagnosis was 28.85±29.88 days.

Isotope scan was available to 79 patients, 73.7% of whom were normal, 10.5% had ectopic thyroid, 10.5% had thyroid agenesis, and 6.3% were goitrous. Permanent congenital hypothyroidism was confirmed in 68.5% of the participants, while 31.5% had transient congenital hypothyroidism. Disease control was sufficient, relative, and insufficient in 78.9%, 14.8%, and 6.3% of the patients, respectively.

According to the findings, 10 patients (6.45%) had abnormal ABR. Among the patients with permanent congenital hypothyroidism, seven cases (6.6%) had abnormal ABR, while only three patients (6.1%) with transient congenital hypothyroidism had abnormal ABR. Among the mentioned 10 patients, seven cases were male.

The association of gender and SNHL in the patients with congenital hypothyroidism was not statistically significant (P=0.4). Abnormal ABR was observed in eight patients with primary congenital hypothyroidism and two patients with central congenital hypothyroidism; however, the difference was not statistically significant (P=0.165). Among the children with SNHL, eight cases received sufficient disease control, and two cases had relative disease control during the treatment (P=0.724).

Mean primary TSH level was 52.45±39.91 IU/l in the children with SNHL, while it was 38.23±28.03 IU/l in the other children (P=0.355). Mean primary T4 level was 6.07±4.33 µg/dl in the children with SNHL and 6.98±3.40 µg/dl in the other children (P=0.307). Mean age at diagnosis and treatment was 28.50±22.13 days in the children with SNHL and 28.87±30.34 days in the other children (P=0.909).

Discussion

Animal studies have confirmed the key role of thyroid hormones in the development of the inner ear. In mutated animal models, the absence of thyroid hormones at the end of pregnancy and after birth has been reported to cause untreatable hearing loss (17). The association of thyroid dysfunction and hearing impairment in patients with congenital hypothyroidism has been demonstrated in various studies (20-22). Such association has also been reported in children and adolescents with isolated central hypothyroidism (23, 24). Furthermore, there have been reports of permanent SNHL in patients with the delayed diagnosis and treatment of congenital hypothyroidism (23, 25).

In the present study, the prevalence of SNHL was 6.45%. In a case-control study conducted in Isfahan (Iran) on children aged more than four months, the prevalence of hearing loss was 2.3% in the patients with congenital hypothyroidism and 0.2% in the control group using ABR (26). In the research by Vanderschueren et al., which was performed on 45 children with congenital hypothyroidism receiving long-term treatment, 20% of the cases had SNHL in higher frequencies, and hearing aid was prescribed for four patients with severe hearing loss (27).

In this regard, Crifo et al. conducted a study on 46 patients with congenital hypothyroidism, and severe hearing loss was observed in five cases (28). In the study by Rovet et al., 14% of the children with congenital hypothyroidism had SNHL (29). Bellman et al. assessed hearing loss in 38 patients with treated congenital hypothyroidism using ABR, reporting severe hearing loss in two cases. Additionally, 16 children were diagnosed with mild SNHL. Based on the findings of the aforementioned studies, mild hearing loss is possible in some cases of congenital hypothyroidism despite early treatment (30). The discrepancy in this regard may be due to the different types of screening tests for hearing acuity, age at hearing screening test, ethnicity, and genetic factors. On the other hand, the lower rate of hearing loss in the current research compared to the previous studies could be due to the age at hypothyroidism diagnosis and receiving sufficient treatment.

Despite the early diagnosis and improved prognosis of congenital hypothyroidism, SNHL remains a permanent concern in patients, especially those with the severe form of the disease (31). Thyroid hormones and the receptors are believed to play a pivotal role in hearing development in rats and human (32). The absence of thyroid hormones for more than three weeks from the 10th week of pregnancy until two months after birth could permanently damage the cochlear and nervous system in rodents (33). The pattern of inner ear development in humans is similar to that of rodents (34, 35); therefore, thyroid hormone deficiency in the neonatal period may lead to hearing loss, which could be prevented through early treatment (36).

Although hearing loss is relatively prevalent in early treated children with congenital hypothyroidism, it is less severe compared to the cases diagnosed before performing neonatal screening programs. It seems that auditory system development associated with thyroid hormones is

not limited to the postnatal period, but rather, it begins in the fetal period (37). In the present study, no correlation was observed between the quality of congenital hypothyroidism treatment and SNHL. Similarly, Crifo et al. (28) and Wasniewska et al. (24) reported no significant association between hearing loss and time of diagnosis and treatment. In the study by Rovet et al., the age at treatment onset for congenital hypothyroidism in children with hearing loss was significantly higher compared to children with congenital hypothyroidism and normal hearing (22 versus 14 days). However, there were no significant differences in the disease severity and duration between the two groups (29).

Findings of the current research showed no association between the type of congenital hypothyroidism and SNHL. In the study by Wasniewska et al., four patients had bilateral SNHL among 10 patients with central congenital hypothyroidism. Therefore, it could be inferred that SNHL is not limited to primary congenital hypothyroidism and may occur in central congenital hypothyroidism (24).

One of the limitations of the present study was the cross-sectional design. In addition, the auditory steady state response test was not available for the study subjects to confirm the results of screening by ABR. The main strengths of the research were the larger sample size compared to the previous studies in Iran and determining the permanency of congenital hypothyroidism and quality of disease control.

Conclusion

According to the results, the prevalence of SNHL in patients with congenital hypothyroidism was lower compared to the reported rates in other countries, while it was higher than Isfahan (Iran). Therefore, assessment of hearing loss should be prioritized in the infants with congenital hypothyroidism in order to prevent lingual skill impairment and communication disorders.

Acknowledgments

This research was officially registered as a pediatrics specialty thesis at the School of Medicine, Qazvin University of Medical Sciences, Iran. Hereby, we extend our gratitude to the parents and their children for their participation. We would also like to thank the staff of the Center for Clinical Research at Qazvin Children Hospital, affiliated to Qazvin University of Medical Sciences, for assisting us in preparing this manuscript.

Conflicts of interests

None declared.

References

1. Agrawal P, Philip R, Saran S, Gutch M, Razi MS, Agroiya P, et al. Congenital hypothyroidism. Indian J Endocrinol Metab. 2015; 19(2):221-7.
2. Rastogi MV, LaFranchi SH. Congenital hypothyroidism. Orphanet J Rare Dis. 2010; 5:17.
3. Ford G, LaFranchi SH. Screening for congenital hypothyroidism: a worldwide view of strategies. Best Pract Res Clin Endocrinol Metab. 2014; 28(2):175-87.
4. Veisani Y, Sayehmiri K, Rezaeian S, Delpisheh A. Congenital hypothyroidism screening program in Iran; a systematic review and metaanalysis. Iran J Pediatr. 2014; 24(6):665-72.
5. Ordooei M, Rabiei A, Soleimanizad R, Mirjalili F. Prevalence of permanent congenital hypothyroidism in children in Yazd, Central Iran. Iran J Public Health. 2013; 42(9):1016-20.
6. Hashemipour M, Ghasemi M, Hovsepian S, Heiydari K, Sajadi A, Hadian R, et al. Prevalence of permanent congenital hypothyroidism in Isfahan-Iran. Int J Prev Med. 2013; 4(12):1365-70.
7. Ghasemi M, Hashemipour M, Hovsepian S, Heiydari K, Sajadi A, Hadian R, et al. Prevalence of transient congenital hypothyroidism in central part of Iran. J Res Med Sci. 2013; 18(8):699-703.
8. Razavi Z, Mohammadi L. Permanent and transient congenital hypothyroidism in Hamadan west province of Iran. Int J Endocrinol Metab. 2016; 14(4):e38256.
9. Saleh DS, Lawrence S, Geraghty MT, Gallego PH, McAssey K, Wherrett DK, et al. Prediction of congenital hypothyroidism based on initial screening thyroid-stimulating-hormone. BMC Pediatr. 2016; 16:24.
10. Silvestrin SM, Leone C, Leone CR. Detecting congenital hypothyroidism with newborn screening: the relevance of thyroid-stimulating hormone cutoff values. J Pediatr (Rio J). 2017; 93(3):274-80.
11. Clause M. Newborn screening for congenital hypothyroidism. J Pediatr Nurs. 2013; 28(6):603-8.
12. LaFranchi SH, Huang SA. Hypothyroidism. In: Stanton BF, St Geme III JW, Schor NF, Behrman RE, editors. Nelson textbook of pediatrics. 20th ed. Philadelphia: Elsevier Health Sciences; 2016. P. 2665-77.
13. American Academy of Pediatrics, Rose SR; Section on Endocrinology and Committee on Genetics, American Thyroid Association, Brown RS; Public Health Committee, et al. Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics. 2006; 117(6):2290-303.
14. Alemu A, Terefe B, Abebe M, Biadgo B. Thyroid hormone dysfunction during pregnancy: a review. Int J Reprod Biomed (Yazd). 2016; 14(11):677-86.
15. Ahmed RG. Hypothyroidism and brain developmental players. Thyroid Res. 2015; 8:2.

16. Kumar J, Gordillo R, Kaskel FJ, Druschel CM, Woroniecki RP. Increased prevalence of renal and urinary tract anomalies in children with congenital hypothyroidism. J Pediatr. 2009; 154(2):263-6.
17. Mustapha M, Fang Q, Gong TW, Dolan DF, Raphael Y, Camper SA, et al. Deafness and permanently reduced potassium channel gene expression and function in hypothyroid Pit1dw mutants. J Neurosci. 2009; 29(4):1212-23.
18. Lang-Roth R. Hearing impairment and language delay in infants: diagnostics and genetics. GMS Curr Top Otorhinolaryngol Head Neck Surg. 2014; 13:Doc05.
19. Joint Committee on Infant Hearing; American Academy of Audiology; American Academy of Pediatrics; American Speech-Language-Hearing Association; Directors of Speech and Hearing Programs in State Health and Welfare Agencies. Year 2000 position statement: principles and guidelines for early hearing detection and intervention programs. Joint Committee on Infant Hearing, American Academy of Audiology, American Academy of Pediatrics, American Speech-Language-Hearing Association, and Directors of Speech and Hearing Programs in State Health and Welfare Agencies. Pediatrics. 2000; 106(4):798-817.
20. Bizhanova A, Kopp P. Genetics and phenomics of Pendred syndrome. Mol Cell Endocrinol. 2010; 322(1-2):83-90.
21. Brucker-Davis F, Skarulis MC, Pikus A, Ishizawar D, Mastroianni MA, Koby M, et al. Prevalence and mechanisms of hearing loss in patients with resistance to thyroid hormone. J Clin Endocrinol Metab. 1996; 81(8):2768-72.
22. DeLong GR, Stanbury JB, Fierro-Benitez R. Neurological signs in congenital iodine-deficiency disorder (endemic cretinism). Dev Med Child Neurol. 1985; 27(3):317-24.
23. De Luca F, Muritano M, Mamí C, Siracusano MF, Galletti F, Galletti B, et al. Hypoacusis of the perceptive type and congenital hypothyroidism. Ann Pediatr (Paris). 1986; 33(1):35-7.
24. Wasniewska M, De Luca F, Siclari S, Salzano G, Messina MF, Lombardo F, et al. Hearing loss in congenital hypothalamic hypothyroidism: a wide therapeutic window. Hear Res. 2002; 172(1-2): 87-91.
25. Vanderschueren-Lodeweyckx M, Debruyne F, Dooms L, Eggermont E, Eeckels R. Sensorineural hearing loss in sporadic congenital hypothyroidism. Arch Dis Child. 1983; 58(6):419-22.
26. Hashemipour M, Hovsepian S, Hashemi M, Amini M, Kelishadi R, Sadeghi S. Hearing impairment in congenitally hypothyroid patients. Iran J Pediatr. 2012; 22(1):92-6.
27. Vanderschueren-Lodeweyckx M, Debruyne F, Dooms L, Eggermont E, Eeckels R. Sensorineural hearing loss in sporadic congenital hypothyroidism. Arch Dis Child. 1983; 58(6):419-22.
28. Crifò S, Lazzari R, Salabè GB, Arnaldi D, Gagliardi M, Maragoni F. A retrospective study of audiological function in a group of congenital hypothyroid patients. Int J Pediatr Otorhinolaryngol. 1980; 2(4):347-55.
29. Rovet J, Walker W, Bliss B, Buchanan L, Ehrlich R. Long-term sequelae of hearing impairment in congenital hypothyroidism. J Pediatr. 1996; 128(6):776-83.
30. 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(3):215-8.
31. Lichtenberger-Geslin L, Dos Santos S, Hassani Y, Ecosse E, Van Den Abbeele T, Léger J. Factors associated with hearing impairment in patients with congenital hypothyroidism treated since the neonatal period: a national population-based study. J Clin Endocrinol Metab. 2013; 98(9):3644-52.
32. Mullur R, Liu YY, Brent GA. Thyroid hormone regulation of metabolism. Physiol Rev. 2014; 94(2):355-82.
33. Knipper M, Richardson G, Mack A, Müller M, Goodyear R, Limberger A, et al. Thyroid hormone-deficient period prior to the onset of hearing is associated with reduced levels of beta-tectorin protein in the tectorial membrane: implication for hearing loss. J Biol Chem. 2001; 276(42):39046-52.
34. Bryda EC. The Mighty Mouse: the impact of rodents on advances in biomedical research. Mo Med. 2013; 110(3):207-11.
35. Friedman LM, Dror AA, Avraham KB. Mouse models to study inner ear development and hereditary hearing loss. Int J Dev Biol. 2007; 51(6-7):609-31.
36. Schroeder AC, Privalsky ML. Thyroid hormones, t3 and t4, in the brain. Front Endocrinol (Lausanne). 2014; 5:40.
37. Chan S, Kilby MD. Thyroid hormone and central nervous system development. J Endocrinol. 2000; 165(1):1-8.