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A 10-year prevalence of congenital hypothyroidism in Khorramabad (Urban Western Iran)

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Abstract

Background: Congenital hypothyroidism in infants is the cause of mental retardation in children, it can be detected in patient and treated at a relatively cheap rate, preventing patient retard. This study aimed to determine the prevalence of congenital hypothyroidism among Khorramabad children.

Methods: In the present study, we identified all patients who had received levothyroxine prescriptions during the study period (2007–2017). Using this as a congenital hypothyroidism surrogate marker, we considered the congenital hypothyroidism prevalence in children above 3 years.

Results: Of 574 patients who had received levothyroxine during the neonatal period up to 3 years, the results of one-variable logistic regression analysis showed that the chance of temporary disease in children with small thyroid ultrasonography was 62% less, than for those without problems, and this difference was significant. The chance of temporary disease in children who had other cases was 87% less than those without problems, and this difference was statistically significant.

Conclusion: The overall prevalence of congenital hypothyroidism in young patients up to 3 years is 0.143%, these values are at least twice those of previous estimates. This proposes an elevation in autoimmune thyroid disease, which is similitude to the rising prevalence of diabetes type 1, which possibly indicates a rising incidence of autoimmunity in youth.

KEYWORDS
autoimmunity, congenital hypothyroidism, temporary disease

1 | INTRODUCTION

The Neonatal Disease Screening Program in Tehran began in October 2006 (Delavari et al., 2006). Congenital hypothyroidism (CHD) in infants is a preventable cause of mental retardation in children at a low cost, it can be detected in patient and treated at a relatively cheap rate, preventing the mental retardation (Ghasemi & Valizadeh, 2014; Grosse & Van Vliet, 2011). In Iran, unlike in other countries, the incidence of CHD in Tehran province was higher than that of the national level, and one of the main causes in this mountainous area is due to iodine deficiency (Ghasemi et al., 2013; Karamizadeh et al., 2011). Lorestan province is located in the western part of Iran, between 46° 51′ to 50° 3′ east of the Greenwich meridian (Hashemipour et al., 2004), and 32° 37′ to 34° 22′ north latitude from the

equator (Ordookhani, Minniran, Najafi, Hedayati, & Azizi, 2003). According to the definition of WHO, if there is a high Thyroid-stimulating-hormone (TSH) in the neonate sample in more than 3% of cases, there is a deficiency of iodine (Jacobson & Rochette, 2018; Kışlal, Çetinkaya, Dilmen, Yaşar, & Teziç, 2010). National prevalence of CHD is 1 per 370–1,000 live births, and the mean of 428 cases in 100,000 live births (Zeidan et al., 2016). CHD screening test started in Lorestan province, Iran since 2007 (Dalili et al., 2014). In the present study, newborn aged 3 to 5 days were screened for CHD, and sampling was carried out by a dried blood spot on a filter paper from heel stick. This study aimed to determine the prevalence of congenital hypothyroidism among Khorramabad children.

1.1 | Methods

In the present study, a total number of 574 patients who were referred to Madani Hospital clinic from March 2007 to March 2017, the study started with drug treatment instruction to the patients. Patients' variables such as history, laboratory tests, and thyroid ultrasonography were documented. Newborn aged 3–5 days were screened from heel stick, and samples of a dried blood spot on a filter paper were used. TSH values were measured using blood sample. TSH less than 5 was considered to be normal. TSH $\geq$ 5 were introduced for serum sampling. In the serum TSH $\geq$ 10 patients are treated and in serum sample 5 < TSH < 9.9, serum test were repeated at intervals of 2–3 weeks and decision was made until the TSH decreased or increased. Treatment was initiated in all patients with 100 μg dose of levothyroxine at a dose of 10 to 15 μg kg^{-1} day^{-1} on a single dose, preferably early in the morning. The first test was after 15 days, and then 30 days. On the 15th day, T4 was expected to reach normal levels and on the 30th day, TSH reached the normal levels. The test was repeated every 1–2 months until the age of 6 months, and then every 3 months to 3 years of treatment. At the age of 3, considering the development of the brain in children is complete, we can discontinue treatment for 1 month and after a month, a serum T4-TSH was measured for distinguish temporary and permanent hypothyroidism.

TSH < 5 resulted in the discontinuation of the drug permanently, thus, the patient recovered (temporary hypothyroidism), however, they are followed up at an intervals of 3 months, 6 months, and 1 year, and then annually for up to 8 years. If 5 < TSH < 9.9 the test was repeated at intervals of 2–3 weeks until the TSH increased or decreased to normal level. If the TSH $\geq$ 10, treatment continues again and the patient suffers from a permanent CHD.

Thyroid ultrasonography was also performed at the same time to evaluate the thyroid gland location, size, and structure.

1.2 | Screening strategy

1.2.1 | Poor patients' compliance

Patients who show an increase in TSH level in the course of treatment despite the appropriate dosage of the drug are considered as poor compliance patients, and these patients are often diagnosed with structural thyroid abnormalities or hormonal thyroid dysfunction. In these cases, at the age of 3, a thyroid ultrasonography was first performed, in the absence of a thyroid gland, the treatment was not discontinued, and the patient to be permanently under observation, treatment with levothyroxine must be continued and the patient suffers from a permanent CHD.

If thyroid tissue was seen in ultrasonography, there are two methods for evaluation of thyroid function in poor compliance patients:

1. Half dose of drug after a month of serum T4-TSH measurement.
2. At 15 days, the drug was discontinued and T4-TSH was measured again.

1.2.2 | Delivery type

From years 2007 to 2010 the type of delivery was not taken into account. From the year 2010, the type of delivery was recorded; normal vaginal delivery—cesarean section (NVD-CS).

1.2.3 | Parents family relationship

Due to a higher prevalence of hypothyroidism in offspring from familial marriages.

Parents: Grade 3, Grade 4, no ratio, and Unknown.

1.2.4 | Family history of thyroid disease

Mother, father, sister, brother, others (grandfather, grandmother, uncle, aunt).

1.2.5 | Anomalies

Anomalies of the cardiovascular, kidney, auditory in patient with CHD are common. Cardiovascular, auditory, other (ocular anomalies, renal, hydrocephalus, small head circumference, large head circumference).

1.2.6 | Time of foot palm sample collection

First sample in 3–5 days after birth, the second sample from year 2010 for twins, and newborn weight <2,500 g or more

than 4,000 g, hospitalized patient, neonatal jaundice, blood transfusion, antibiotic, other drug use, and TSH ≥ 5 in First sample.

1.2.7 | TSH foot palm

Suspected cases with TSH ≥ 5.

False negative TSH < 5, but in serum sample they were sick patients.

1.2.8 | Baby's age at the start of treatment

Due to the onset of treatment before 21 days, there was no brain damage of newborns.

1.2.9 | Three-year ultrasound or a temporary termination treatment

Ninety-five percent of ultrasonography cases were performed by a skilled ultrasonography expert. The thyroid has been investigated in terms of location, size, and echo status, three of which are normal, abnormal, and unclear.

Uncertainties include: Patients who have not visited, immigrants or those who are still under 3 years of age and no interruption of treatment has taken place.

1.3 | Serum confirmatory test in neonates and CHD classification

Measurement of total T4 and TSH to determine the status of the patients. The serum sample has been recorded with total T4 and TSH. The method of initiating treatment for TSH ≥ 10 or in cases where TSH has not been fixed in several cases between 6 and 9.

1.4 | Diagnostic reevaluation at 5–10 years of age of CHD with thyroid gland in situ (GIS)

1.4.1 | Treatment process

Discontinue treatment after 3 years of treatment and discontinuation of 1 month treatment and normalization of the tests. Unspecified lack of referral and immigration. Treatment has been associated with increased TSH after 3 years of interruptions, or those who are still 3 years old whose treatment have not been interrupted. It should be noted that the patient were 3 years old until 2013 and their status was determined.

1.4.2 | Date of interruption of treatment

In most cases, it is 3 years old, but cases that have improved earlier are included in the column of treatment.

2 | RESULTS

People with a first-degree relative history (family) have a 40% lower chance of having a temporary type of disease than those without a family history. As well as those with a family history of other people, 48% fewer than those with no familial history had the chance of having a temporary type of disease.

The odds of being sick were temporary in those who had a third degree relatives, 21% were less likely to be related. As well as the chance of having a temporary illness in those who had a fourth-degree relative, 62% were less likely to have relatives.

The chance of recovery (temporary type of disease) in children born with cesarean section was 1.7 times that of children born with normal vagina delivery.

The chance of recovery in males was 1.26 than females. However, this ratio was not statistically significant.

The chance of having a temporary disease in those who did not have anemia was 2.8 times than those with anemia and this difference was also significant.

The chance of recovery (temporary) in those who did not have prolonged jaundice was 1.7 times that of prolonged jaundice, but this difference was not significant.

The odds of transient disease in those with no chromosomal abnormalities were more than 3.5 times those who had a chromosomal disorder but this difference was not significant at 5%.

We changed the type of thyroid problem in sonography to the category so that: (a) No problem (b) Small thyroid in sonography (c) Sonography agenesis, and (d) We compiled other items into one category due to the very low frequency underneath the different groups (Table 1).

We showed the number and frequency of each group by the final outcome of the disease (temporary and permanent) in the above tables. The results of one-variable logistic regression analysis showed that the chance of temporary disease in children with small thyroid ultrasonography was 62% less than the chance for those without problems, and this difference was significant. In the group of children with thyroid gland problem, because of the fact that all of these children had a permanent illness, the odds ratio could not be calculated (a meaningless number). Also, the chance of transient disease in children who had other cases was 87% less than the chance for those without problems, and this difference in luck was statistically significant.

The chance of recovery (temporary type of disease) did not depend on the age at which treatment began.

The cut-off point for TSH was 1.7. Both sensitivity and specificity were reported according to this cut point of 0/96. It should be noted that 28% of cases that were of a permanent type of disease were unidentifiable by considering the standard cutting point before 5 (Table 2 and Figure 1).

TABLE 1 Type of problem in Sonography

	Permanent disease	Temporary disease	Total
Types of thyroid problem			
Without problem			
Count	63	213	276
Expected Count	90.2	185.8	276.0
Small Thyroid in Sonography			
Count	14	18	32
Expected Count	10.5	21.5	32.0
Thyroid agenesis			
Count	28	0	28
Expected Count	9.1	18.9	28.0
Other cases			
Count	9	4	13
Expected Count	4.2	8.8	13.0
Total			
Count	114	235	349
Expected Count	114.0	235.0	349.0

TABLE 2 Classification of patients into two types of transient and permanent hypothyroidism

	Permanent	Transient
TSH > 7.1	3	216
TSH < 7.1	83	12
TSH > 5	2	165
TSH < 5	82	63

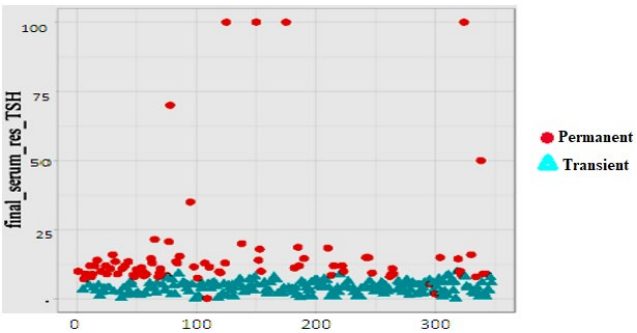

FIGURE 1 Distribution chart of the level of TSH in patients according to the type of disease

3 | DISCUSSION

People with first-degree family members (families) have a 40% lower chance of having a temporary type of disease than those without a family history (Jones & Rose, 2018). Those with a familial history of others, 48% had a lower chance of having a temporary type of disease than those without a familial history (Shareef et al., 2018).

The chance of having a temporary disease was lower in those who had a grade 3 relationship, 21% from those without a familial relationship. The chance of having a temporary illness in those who had a fourth grade relative of 62% was less than those who had no familial relationship.

The chance of recovery (temporary type of disease) in children born with CS was 1.7 times that of children born with NVD. The chances of recovery were 1.26 for girls in comparison with boys, although this ratio was not statistically significantly different.

The chance of having a temporary disease in those who did not have anomaly was 2.8 times more likely than those with anomaly, and this difference was also significant. The chance of recovery (temporary) in those who did not have prolonged jaundice was 1.7 times than those with prolonged jaundice, but this was not significant. The odds of temporary disease in those with no chromosomal abnormalities were 3.5 times more than those who had a chromosomal disorder, but this difference was not significant at 5%.

We changed the type of thyroid problem in ultrasonography into four categories: Healthy, small thyroid in ultrasonography, thyroid genesis and we compiled other items into one category due to the very low frequency underneath the different groups.

We showed the number and abundance of each group in terms of the outcome of the disease (temporary and permanent) in the tables above. The results of one-variable logistic regression

analysis showed that the chance of temporary disease in children with small thyroid ultrasonography was 62% less than the chance for those without problems, and this difference was significant. In the group of children with thyroid genes, because of the fact that all of these children had a permanent illness, the odds ratio could not be calculated (the number is meaningless).

Also, the chance of temporary disease in children who had other cases was 87% less than the chance for those without problems, and this difference in luck was statistically significant. BMI did not affect the chance of responding to patients' treatment. The chance of recovery (temporary type of disease) did not depend on the onset of treatment.

4 | CONCLUSION

The overall prevalence of CHD in newborn patients under 3 years is 0.143%; these values are at least twice those of previous estimates. This proposes an elevation in autoimmune thyroid disease, which is similar to the rising prevalence of diabetes type 1, which possibly indicates a rising incidence of autoimmunity in youth.

CONFLICT OF INTEREST

The authors deny any conflict of interest in any terms or by any means during the study. All the fees provided by research center fund and deployed accordingly.

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