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The Prevalence of Congenital Hypothyroidism in Rafsanjan in Southeast Iran during 2017-2019

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Abstract

Background: Congenital hypothyroidism (CH) is one of the most common endocrine diseases in newborns. Epidemiologic studies are very important to carry out more preventive assessments. This study evaluated the prevalence of CH in Rafsanjan in southeast Iran during 2017-2019.

Materials and Methods: In this descriptive study, we used the data collected from the CH screening of newborns in Rafsanjan, Kerman Province, Iran. The study population was 18832 newborns who had undergone a CH screening program according to the standard CH screening protocol in a public health center from March 2017 to March 2019. Diagnosed CH cases were compared with healthy newborns using chi-square.

Results: Overall, among this population, 94 cases were diagnosed with CH during the years 2017 to 2019. The prevalence of CH in Rafsanjan city was 4.99 per 1000 live births during 3 years. The frequency of thyroid dysfunction in the mother and birth weight under 2500 were higher among the CH group than the non-CH group ($P < 0.001$).

Conclusions: The study findings showed that the frequency of thyroid dysfunction in the mother and birth weight under 2500 were higher among the CH group than the non-CH group. Further studies with individual data and longitudinal are suggested to be more confident about the causality of the association.

Keywords: Congenital Hypothyroidism, Prevalence, Neonatal Screening, Iran.

Introduction

Congenital hypothyroidism (CH) is one of the most common endocrine diseases in newborns. The incidence of CH has increased globally with the increased use of neonatal screening programs. However, the related factors of CH have not been completely elucidated [1]. Thyroid hormone deficiency in infants causes mental retardation unless proper diagnosis and treatment is started early in the life of the infant [2]. The hypothalamus-pituitary-thyroid axis works in the middle of fetal life and develops until full-term birth. If there is hypothyroidism in the fetus, important organs such as the central nervous system and skeleton will experience some degree of disorder [2]. Babies with hypothyroidism mostly have a normal appearance. At the time of delivery, clinical symptoms are few and non-specific due to the placental transfer of maternal thyroid

hormone and the increase in brain iodothyronine deiodinases (an enzyme that converts T4 to T3). Therefore, less than 5% of babies are diagnosed with clinical examination symptoms before the screening report [3].

In general, the average prevalence of this disease in Iran is estimated to be 1 in 1000 cases, while its prevalence in the world is 1 in 3000-4000 [4], which indicates the high prevalence of this disease in Iran. The first screening of CH in a large population was performed in 1974 in Quebec, Canada [5]. In Iran, the screening program was first performed in 1987 by Azizi et al [6] and has been running in the health systems of Iran since 2005 [7].

Epidemiologic studies are very important to carry out more preventive strategies, especially in areas with a high rate of CH [8]. Based on previous findings, several individual and environmental factors, including gender, birth weight, race, maternal age, parental education, type of delivery, birth order, being twins, and drug use during pregnancy, may affect CH, but there is no agreement on some of the possible related factors. It is believed that many other related factors may influence the prevalence of CH, and identification of these factors may help reduce the prevalence of CH [8, 9].

The prevalence of CH in the Rafsanjan region is unknown. Previous studies in Kerman province showed the prevalence of CH in infants was 3.4 per 1000 infants [10] to 7.4 per 1000 infants [11]. Considering the high prevalence of CH in Kerman province and its importance in intellectual disability, and given that having a higher index of suspicion for CH in infants can be useful in identifying them, this study aimed to determine the prevalence of CH and some related factors in infants referred to the screening center of Rafsanjan University of Medical Sciences during 2017-2019.

Materials and Methods

In this descriptive study, we used the data collected from the CH screening of neonates at Rafsanjan University of Medical Science, Kerman Province, Iran. The inclusion criteria were neonates who had undergone a CH screening program according to the standard CH screening protocol in a public health center from March 2017 to March 2019 in Rafsanjan. The study population was 18832 neonates. All those who did not suffer from CH were regarded as controls in this study. During 3-5 days of birth, blood samples from heel pricks were collected on 903 Whatman filter papers by trained staff. The dried samples were immediately sent to the screening laboratory of the province via express mail. The enzyme-linked immunosorbent assay (ELISA) method measured Thyroid-stimulating hormone (TSH). Following the national screening program protocol, the level of the first TSH measurements higher than 5 mu/L in neonates aged 3-7 days was defined as abnormal. These cases were recalled for further evaluation, and additional confirmation tests [thyroxine (T4), TSH, and triiodothyronine resin uptake (T3RU)] were performed. The second measurement was performed between 7 and 28 days of birth. If the T4 level was < 6.5 µg/dL and the TSH level was > 5 mIU/L, the neonates were defined as hypothyroid. In CH cases, variables such as gender, birth weight, nationality, delivery type, maternal age, residency, and maternal history of thyroid disorder were recorded individually.

The maternal and neonatal information of healthy newborns (as aggregation data) was extracted from the Integrated Health System (IHS) of the health center of Rafsanjan. The SIB IHS system was designed and implemented to record, maintain, and update Iranian electronic health record information. Maternal and neonatal-perinatal factors regarding newborns with CH were extracted from medical records when they had undergone CH screening in a public health center. In the present study, all born babies who did not suffer from CH were regarded as controls.

Descriptive statistics such as frequency (%) for categorical variables were used and selected factors in neonates were compared across the groups of our study using chi-square. Data were analyzed using SPSS version 20 software. A significance level of 0.05 was also considered.

Results

In this study, 18,832 neonates who had undergone a CH screening program according to the standard CH screening protocol in a public health center from March 2017 to March 2019 in Rafsanjan were included in the study. Among them, 94 cases were diagnosed with CH and included in the case group; the rest were considered as controls. The prevalence of CH from 2017 to 2019 in Rafsanjan was 4.99, 4.26, and 5.81 per 1000 live births, respectively (4.99 per 1000 live births during 3 years) (Table 1).

Table 1. Prevalence of congenital hypothyroidism (CH) in infants born in Rafsanjan during 2017-2019

Year of birth	Total births	With CH	Prevalence of CH *
2017	6816	34	4.99
2018	6333	27	4.26
2019	5683	33	5.81
Total	18832	94	4.99

* Per 1000 live birth

Table 2 shows some selected demographic and medical factors in infants with and without CH. From the total population, 0.43% of boys and 0.58% of girls had CH. The prevalence of CH in infants with a family history of thyroid dysfunction in the mother was significantly higher than in infants without this disease in the mother (0.93% vs. 0.45%). Also, infants weighing less than 2500 had significantly the highest frequency of CH compared to other groups. The prevalence of CH in babies with birth weight less than 2500, >3500, and 2500-3500 grams was 1.06, 0.61 and 0.4%, respectively. The present study showed that the frequency of CH was not different between the CH group and control group in terms of gender, place of residence, type of delivery, maternal age, and nationality (P >0.05).

Table 2. Some selected related factors in neonates with and without congenital hypothyroidism (CH) born in Rafsanjan during 2017-2019 (n=18832)

Variables		Total (n=18832)	Without CH (n=18738)	With CH (n=94)	P-value
		N(%)	N(%)	N(%)	
Gender	Male	9986(100)	9943(99.57)	43(0.43)	0.149
	Female	8785(100)	8734(99.42)	51(0.58)	
	missed	61(100)	61(100)	0	
Residency	Urban	12498(100)	12441(99.54)	57(0.46)	0.513
	Rural	6273(100)	6240(99.47)	33(0.53)	
	missed	61(100)	57(93.44)	4(6.56)	
Delivery type	Vaginal	9721(100)	9672(99.50)	49(0.50)	0.229
	Cesarean	9050(100)	9015(99.61)	35(0.39)	
	missed	61(100)	51(83.61)	10(16.93)	
Thyroid disease in mother	No	16938(100)	16861(99.55)	77(0.45)	0.006
	Yes	1833(100)	1816(99.07)	17(0.93)	
	missed	61(100)	61(100)	0	
Maternal age (years)	<18	433(100)	433(100)	0	0.242
	18-35	14801(100)	14726(99.49)	75(0.51)	
	<35	3525(100)	3511(99.60)	14(0.40)	
	missed	73(100)	68(93.15)	5(6.85)	
Weight (grams)	<2500	1881(100)	1861(98.94)	20(1.6)	<0.001
	2500-3500	14601(100)	14543(99.6)	58(0.40)	
	>3500	2289(100)	2275(99.39)	14(0.61)	
	missed	61(100)	59(96.72)	2(3.28)	
Nationality	Iranian	14926(100)	14853(99.51)	73(0.49)	0.655
	Non-Iranian	3845(100)	3824(99.45)	21(0.55)	
	missed	61(100)	61(100)	0	

Discussion

Given the prevalence of CH in Kerman province and its importance in intellectual disability, this study aimed to assess the prevalence of CH among infants referred to the screening center of Rafsanjan University of Medical Sciences during 2017-2019. CH among infants in Rafsanjan increased in 2019 compared to 2017. This finding was consistent with a study by Liu et al. that reported that CH's global prevalence increased from 1969 to 2020 after controlling for the effects of geographic area, national economic level, and screening protocol [12]. In contrast, an increasing trend in the incidence of CH was not observed in the study of Taheri et al. in Iran [13].

The prevalence of CH in the present study was 4.99 in 1000 births. The prevalence of CH varies from place to place. In a study conducted by Doustmohamadian et al. in Semnan province, Iran, the prevalence of CH was 6 per 1000 [12]. On the other hand, studies in Fars [7] and Guilan [13] in Iran have shown that the prevalence of CH is 1:1465 and 1 in 542, respectively. It has been reported to be 1:2000 in China [14], 1:2500 in Japan [15], and 1 in 2000-3000 in Italy [16]. These statistics show that the prevalence of CH in Rafsanjan is higher than the world average. Therefore, given the importance of this disorder in causing mental retardation, it seems necessary to increase parents' knowledge about CH and encourage them to participate in the screening plan for CH. The variation in CH prevalence among countries may be due to differences in iodine levels in different geographical regions, differences in climate, living conditions, autoimmune factors, various environmental and genetic factors, different study designs and also, and various screening protocols.

The results of the present study showed that the frequency of CH was higher in the neonates of the mothers with thyroid dysfunction than in the newborns whose mothers didn't have thyroid dysfunction (0.93% vs 0.45%), which was consistent with a previous study in Sanandaj, Iran [17]. Therefore, a family history of thyroid disease should be considered an important factor and included in the maternal control program. Increasing mothers' awareness about thyroid dysfunction can be greatly helpful in identifying

vulnerable groups and creating some programs to prevent and control CH.

The results of this study showed that the prevalence rate of CH in neonates born with birth weight < 2500 gr was higher than that in newborns with normal weight (1.6% vs 0.4%). It may be due to the higher risk of iodine deficiency in low birth weight babies. This finding was inconsistent with the findings of some previous studies [18-22] that differed in study design and data analyzing method. However, a study conducted in Guilan province in Iran [13] found similar results. Considering the necessary care and education about the mother's nutrition during pregnancy is suggested.

The present study revealed no significant difference between CH and control groups regarding gender. However, in the study performed by Abedi et al. in Sanandaj, Iran [17], the frequency of CH in male neonates was higher than that in female ones. On the contrary, some previous studies have shown that the risk of CH was higher in female neonates after adjusting the confounding variables [1, 18].

Furthermore, the present study showed that the frequency of CH was not different between the CH group and control group in terms of place of residence, type of delivery, maternal age, and nationality. Inconsistent with the present study that used aggregation data, other studies with individual data found significant associations. For example, in the study by Zhou et al. in China, the incidence of hypothyroidism was associated with maternal age [1]. The results of a study in Khorasan Razavi Province, Iran, showed that after adjusting the effects of other variables, the odds of CH were higher by 79% and 44% in rural and suburban areas, respectively, compared to urban areas [8]. On the other hand, Keshavarzian et al. found that the risk of CH was 3.4 times higher in neonates born in urban areas compared to newborns born in rural areas [21].

The current study was a population-based study. However, there were limitations. One of the limitations of the present study was the simultaneous evaluation of CH and its related factors. So, it was not possible to investigate the temporal relationships accurately. Another limitation of the present study was its retrospective design. Therefore, other potential factors, such as maternal medical history, were unavailable. Finally, the individual data were not available in the present study, So we could not adjust the effects of confounders using multiple logistic regression analysis.

Conclusion

The study findings showed that the prevalence of CH in infants with a family history of thyroid dysfunction in the mother and infants weighing less than 2500 was significantly higher than control groups. However, further studies with individual data and longitudinal are needed to be more confident about the causality of the relationships. According to the present results, timely screening of CH in mothers with thyroid dysfunction and mothers with an abnormal weight baby is of great importance.

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Conflict of interest

None declared.

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Ethical Considerations

The participants' data were kept confidential and were only accessible to the researchers.

Code of Ethics

This study was confirmed by the Ethics Committee of Rafsanjan University of Medical Sciences (Ethics code: IR.RUMS. REC.1398.195).

Authors' Contributions

Hajar Vatankhah: Designed the study and supervised the project, wrote the initial paper. Hassan Ahmadinia: Performed the statistical analysis, wrote the initial paper. Mina Asadikaram: Collected data, wrote the initial paper. Batool Rezaei: Collected data. Mohsen Rezaeian: Performed the statistical analysis. Zahra Jamali: Wrote the initial paper. All the authors read and approved the final manuscript.

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