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Congenital Hypothyroidism: Increased Incidence in Yazd Province, Iran

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Abstract:

Introduction: Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation. Its worldwide incidence is estimated to be one in 2500-5500 births. Assessment of thyroid gland in neonates is critical. The aims of this study were to demonstrate the incidence of CH in neonates born in Yazd province, Iran in 1389 (2010) and compare the results with other reported studies and investigate biochemical characteristics of affected infants.

Materials & Methods: This is an analytical descriptive cross-sectional study. The study was conducted on all infants (13022 births) born in 1389 (March 2010-March 2011). Thyroid stimulating hormone (TSH) was measured using ELISA technique.

Results: Forty five infants suffered from congenital hypothyroidism with an overall incidence of one in 289 live births. Twenty five of the diagnosed infants were males (incidence 1:261) and twenty were females (incidence 1:325). The incidence of CH in boys was more than girls (P-value = 0.295). The highest incidence of CH was observed in spring followed by summer and the lowest incidence was in autumn followed by winter (P-value=0.000.

Conclusion: The CH incidence was 10.3 to 13.8 times more than other countries. The highest CH incidence was in spring followed by summer and the lowest incidence was in autumn followed by winter. It is important that a larger size of cases need to be screened and more information on the aetiology of the affected infants to be obtained.

Keywords: Congenital Hypothyroidism, Incidence; Intellectual Disability; Thyroid Gland; Infants

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Introduction

Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation[1]. Most cases of CH are not hereditary and result from thyroid dysgenesis[2]. Some forms of thyroid dysgenesis (aplasia, hypoplasia, or an ectopic gland) are the most common cause of CH, accounting for 85% of cases; 10% are caused by an inborn error of thyroxin synthesis, and 5% are the result of transplacental maternal thyrotropin-receptor blocking antibody (TRBAb)[3, 4].

The most common form of thyroid dysgenesis is an ectopic gland, which is mostly detected by newborn screening. A variety of defects in the biosynthesis of thyroid hormone may result in CH. A goiter is always present. When the defect is incomplete, compensation occurs, and onset of hypothyroidism may be delayed for years [3].

The most common type of the T_4 synthesis defect is thyroid peroxidise defect of organification and coupling. After iodine is trapped by the thyroid, it is rapidly oxidized to reactive iodine, which is then incorporated into tyrosine units on thyroglobulin. This process requires generation of H_2O_2, thyroid peroxidase, and hematin (an enzyme cofactor); defects involve each of these components, and there is considerable clinical and biochemical heterogeneity [5].

Maternal thyrotropin receptor-blocking antibody (TRBAb) is an unusual cause of transitory CH. Trans-placental passage of maternal TRBAb inhibits binding of TSH to its receptor in the neonate. Deficiency of TSH and hypothyroidism may occur in any of the conditions associated with developmental defects of the pituitary or hypothalamus. More often in these conditions, TSH deficiency is secondary to a deficiency of thyrotropin-releasing hormone (TRH) [3, 6].

Congenital causes of hypothyroidism are categorized as sporadic or familial, goitrous or nongoitrous. In many cases, thyroid hormone deficiency is severe, and symptoms develop in the first weeks of life. In others, lesser degrees of deficiency occur, and manifestations may be delayed for months [6]. Its incidence worldwide is known to be one in 2500-5500 births. In some ethnicities such as Hispanic, its incidence is one in 2000 births [7]. The incidence in Japan and North America in which people consume adequate iodine is one in 7000 and 4250 births, respectively [8]. So, assessment of thyroid gland in neonates is very important. Most newborn screening programs measure T_4 levels, followed by measurement of TSH when T_4 is low [7, 9].

Now, in majority of countries, screening for CH in neonates is a part of national screening programme. The screening programme has prevented some mental retardation which has led to decreased economic and sociologic bearings of CH [10]. The screening programme performed in developed countries helped to study the aetiology and pathogenesis of CH [11-14].

The surveys in different parts of Iran reported different incidences for CH, i.e. one in 914, 1433, and 370 births in Tehran, Shiraz and Isfahan, respectively [15]. The incidences in all cities are more than worldwide incidence.

The aim of this study was to demonstrate the incidence of CH in neonates who were born in Yazd province, Iran in 1389 (2010). The second aim was to compare the results with the other reported studies and investigate biochemical characteristics of affected

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infants. Then, these data can be utilized for performing preventive actions in different levels.

We now present data from the regional screening programme in Yazd province, which is situated in the centre of Iran and has a population of 960000 with an annual birth rate of 13022(#13/1000).

Materials & Methods

This is an analytical descriptive cross-sectional study. The study was conducted on all infants (13022 births) born in Yazd in 1389 (March 2010-March 2011). Blood samples from all the newborns spotted on a Whatman 903 filter paper on the third, fourth, and fifth days of life. The samples were collected from 38 health centres held on 10 cities of Yazd province. Then, the samples were processed at Yazd Central Laboratory. During transportation, samples were kept in insulated containers.

Thyroid stimulating hormone (TSH) was measured using ELISA technique. TSH less than 5mu/l and 4mu/l were considered normal for 3-7 day-old and ≥8 day- old neonates, respectively. Then, the neonates with TSH more than normal were selected. Their samples were collected and measured for T4, TSH, and T3 RUP. Infants with T4 less than 6.5 µg/dl or TSH more than 10 mu/l were included in this study. A standard detailed questionnaire was prepared with the help of epidemiology department of Shahid Sadoughi University of Medical Sciences. The results were analysed using SPSS software with applying statistical testes such as chi-square. A confidence level of 95% was considered for the results.

Results

The total number of 13022 newborn infants were screened, among whom 6527 (%50.1) were males and 6495 (%49.9) were females. The newborn infants' weights were between 1000-5800 grams with the mean of 3139.8 g. Mean mothers' age was 25.8 ± 5 years.

Table 1 shows the distribution of TSH rates in male and female infants. Recall rate was about 6.17% and so 803 neonate's serums were examined for T4, TSH and T3RUP.

Forty five infants have congenital hypothyroidism with an overall incidence of one in 289 live births. Twenty five of the diagnosed infants were males (incidence 1:261) and twenty were females (incidence 1:325).

The incidence of CH in boys was more than girls; However, the difference was not statistically significant (P = 0.295).

Mean weight of neonates was 3139g and 3203g in normal and CH diagnosed cases, respectively; The difference was not significant (P = 0.357)

The average age of the infants' mothers was 25.85 and 26.22 years in normal and CH diagnosed cases, respectively. The difference between them was not significant (P = 0.643). %83.2 and %16.8 of the infants lived in rural and urban areas, respectively. CH incidence on the rural and urban areas was 1:315 and 1:216 live births, respectively; and the difference was not significant (P =0.295).

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Table 1: The frequency distribution of TSH levels in males and females

TSH Level	Male		Female		Total	
	N	%	N	%	N	%
<4	5570	88.03	5829	89.74	11399	88.90
4≤ 5	406	6.42	361	5.56	767	5.98
5≤ 9.9	325	5.14	292	4.50	617	4.81
10≤ 19.9	14	0.22	10	0.15	24	0.19
20≤	12	0.19	3	0.05	15	0.12
Total	6327	100	6495	100	12822	100

Table 2 shows the distribution of the average seasonal incidence rates of CH in different seasons. The highest incidence of CH was observed in spring followed by summer and the lowest incidence was observed in autumn followed by winter, and the difference was statistically significant (P=0.000).

Table 2: The frequency distribution of average seasonal incidence rate of CH

Season	CH	
	Number	Incidence
Spring	18	1 in 95 births
Summer	15	1 in 250 births
Autumn	2	1 in 1934 births
Winter	10	1 in 369 births
Total	45	1 in 289 births

Discussion

The incidence of CH in this study in Yazd province in 1389 (March 2010-March 2011) was found to be one in 289 newborn infants, a figure far higher than that reported from other provinces in Iran, and that reported worldwide. The CH incidence is 10.3 to 13.8 times more than other countries which are performing routine national screening programme [16]. CH incidence is different in different countries, e.g. 1:67 in Nigeria [17], 1:781 in Pakistan [18], 1:2736 in Turkey [19] and 1:10000 in black American population [20]. The reported CH incidence in different parts of Iran was different and all of them found a higher incidence in comparison to the worldwide reports [21, 22, 23].

There are many reasons [23] for the differences between incidences including using T4 or TSH measurement alone for screening, different thresholds for diagnosis of CH, iodine deficiency in some parts of the world, ethnic differences i.e. CH incidence in Turkey is 1:2943, in Saudi Arabia 1:2759, in Japan 1:7000, and in Arabs live in Israel is 1:1447 which is more than that in non-Arab population of Israel (1:2070). The other reasons are use of iodine-containing antiseptics (especially in immature

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neonates) and heredity and environmental factors. Whereas the laboratory test results of %40 of CH-diagnosed neonates became normal, their drug treatment discontinued. They were placed in the group with transient hypothyroidism. After three years, it can be decided about the number of cases with transient hypothyroidism. CH incidence is very high in Yazd province and so its causes need to be studied. Although based on IDD programme report Yazd province population is not suffering from iodine deficiency. However, because of high CH incidence, it needs to be precisely surveyed for iodine deficiency.

The majority of studies showed that CH incidence in female neonates is more than male neonates. Female to male ratio in Saudi Arabia [24], Estonia [25] and China [26] is 1.8:1, 4:1, and 1.5:1, respectively. In this study the female to male ratio was 1:1.25, which is completely different from other studies.

In this study, the highest CH incidence was observed in spring followed by summer and the lowest CH incidence was in autumn followed by winter. Significant seasonal differences in CH incidence have been reported in some countries. For example significantly higher incidences of CH were seen in the summer in Japan, in the winter in Australia and Quebec. In other countries such as Norway, Switzerland and France, no significant peaks have been reported [27, 28].

Finally, it is important that a larger size of cases to be screened and more information on the aetiology of the affected infants be obtained.

So far, the current background information is critical for appropriate counselling such as genetic counselling in these cases.

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