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Original Research Article

Screening for congenital hypothyroidism: results of screening 5600 Ardabil province infants

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ABSTRACT

Background: Congenital hypothyroidism (CH) is a condition of thyroid hormone deficiency which varies more by geographic areas and affecting 1 in 3000 to 4000 of newborns. The aim of this study was to investigate the screening of CH results in in Ardabil Province, Iran.
Methods: This descriptive study was conducted on 158624 neonates during 2007 to 2013 which were screened for CH by measuring serum TSH obtained by heel prick. Of all neonates 5600 neonates who had a TSH ≥5 mU/L were recalled for measurement of serum T4 and thyroid stimulating hormone (TSH) in venous samples. Collected data analyzed by statistical methods in SPSS.16.
Results: The incidence of congenital hypothyroidism was found to be 1:916 with a female to male ratio of 0.76:1. In 220 patients with CH, 40 patients were diagnosed with permanent CH (18.2%) and 140 with transient hypothyroidism (81.8%). The frequency of transient hypothyroidism was 4.5 times more than permanent hypothyroidism and was significant. In newborns with permanent hypothyroidism the average of TSH levels in the first and second times was 37.15 and 31.56 µIU/ml, respectively.
Conclusions: Results showed that the prevalence of CH in Ardabil province was significantly high and comparing the results of this study with other studies in other countries suggests the proper efficacy of congenital hypothyroidism screening in Ardabil's health system. Also we should be attention to other environmental factors especially during pregnancy which affect the performance of the mother's thyroid.

Keywords: Congenital hypothyroidism, Prevalence, Screening, Ardabil

INTRODUCTION

One of the hormones involved in human development, especially the development of the nervous system of the thyroid hormones.[1,2] So early diagnosis and treatment of hypothyroidism can prevent mental retardation in congenital defects of these hormones.[3]

For the prevention and treatment of neurological disorders and mental retardation in hypothyroidism over the last decade, many efforts have been done in low developed or underdeveloped countries.[4,5]

Before the onset of the screening system (until 1970), more than a third of children with hypothyroidism were not diagnosed for a long time and in the years after the infancy they experienced severe mental and nervous disorders and at this step was no possibility of treatment and prevention of the disease so that the delay in diagnosis and treating of hypothyroidism for 5 to 6 months cause to reduce the level of intelligence of individuals below 70 (IQ<).[6,7]

In the province of Ardabil, the program for the screening of congenital thyroid disease began in late 2006 at the

same time as a national screening program. Before the onset of the neonatal screening program, the incidence of congenital hypothyroidism, which was diagnosed with clinical manifestations, was between 1:7000 and 1:5000 with the onset of neonatal screening, the incidence ranged reached to 1:3000 to 1:4000 live births. By increasing the experience of health systems and performing a global screening program, it seems that hypothyroidism to be different based on geographic areas and more than this amount.[8]

In a report from France based on a neonatal screening system over the 20 year, the prevalence of congenital hypothyroidism was 1:1000 live birth and in a report from Greece over the 11 years of screening, the prevalence was much higher and was about 1:800 birth.[9,10]

According to reports, in the United States neonates, the incidence of congenital hypothyroidism has risen from 1:4094 in 1987 to 1:2372 live births in 2002 which the reason for this increase unknown but researchers consider the progress of laboratory assessment and evaluation tools as one of the reasons for the accurate determination of thyroid hormones levels which has increased the prevalence in this interval.[11]

By increasing sensitivity and validity of TSH level measurement methods in many screening systems in the world and in the United States, measuring the level of the T4 hormone has changed to TSH level measurements. By pull down the cut off level of TSH many infants with mild congenital hyperthyroidism has been diagnosed. In addition, TSH level changes in many geographic areas and races of population has not difference and is suitable for screening. In many US screening systems for Asian migrant population a high prevalence of congenital hypothyroidism has been reported but among African Americans this prevalence has been very low and in totally, the prevalence of hypothyroidism among white populations is reported more than blacks. In the screening program in New York during the years 2000 to 2003, the incidence of congenital hypothyroidism was generally 1:1613 and among boys was 1:1763 and girls were 1:1651. In cases with the birth weight between 1500 g and 2500 g, the prevalence was higher and reached to 1:851 live births and under 1500 gr the birth weight, the prevalence was 1:1396.[11] The aim of this study was to evaluate the results of permanent and transient congenital hypothyroidism screening in Ardabil province.

METHODS

This descriptive study was conducted in health centers of Ardabil province on infants born during 2007 to 2013 (158624 live birth) that out of them 5600 cases were recalled for evaluation again.

According to the country congenital hypothyroidism screening program is performed using a neonatal hepatocellular blood sample that occurs 3 to 5 days after birth and TSH is measured by ELIZA and is considered normal if TSH is less than 5 mU/L. If the result of the TSH was between 5 and 9.9 mU/L, in age 4 weeks, TSH, T3RU and T4 were checked for infants by getting intravenous blood sample of them.

If the result of the TSH test was between 10 and 9.9 mU/L, a blood sample is given at 2 to 3 weeks and if the primary titer is greater than or equal to 20 mU/L then intravenous testing is immediately checked and if the initial titer is greater than or equal to 20 mU/L then venous testing is immediately checked and treatment with Levothyroxine is prescribed. If the venous T4 test is less than 6.5 µg / dL and TSH is greater than 20 mU/L, a diagnosis of hypothyroidism is given and the treatment begins or continues if it has already begun.

In this study, cases with TSH equal 5 mU/L or more were considered as Recall samples. The cases of hypothyroidism were diagnosed and after 3 years of hypothyroidism and were considered as congenital hypothyroidism and its frequency in the total screened population was calculated. Finally at the end of the 3 year or for any reason prior to thyroxine administration and had normal thyroid function were considered congenital hypothyroidism. The collected data were analyzed by SPSS v16 using statistical methods including Chi-square and T-test and descriptive statistics methods in the form of table and diagram. In all tests a significant level was set as $p<0.05$.

RESULTS

Of all recall infants, 220 (3.9%) neonates based on screening results and TSH amount were suffered to congenital hypothyroidism.

The incidence of congenital hypothyroidism (transient and permanent) in Ardabil province was 1 patient in 916 live births. Of the total number of patients 180 cases (81.8%) of transient hypothyroidism and 40 cases (18.2%) of permanent hypothyroidism were followed up for 1 year. Of these 180 infants, 102 newborns (56.7%) were female.

Table 1: Socio-demographic data of patients.

Variables		n	%
Sex	Girl	102	56.7
	Boy	78	43.3
Family history (+)		117	60.9
Mean±SD			
Weight		3.2±0.5	
Height		49±3.1	
TSH in first time		29.7±26.7	
TSH in second time		30.6±28	

Table 2: Growth indexes of infants with congenital hypothyroidism.

Variables	Birth time	1 month	4 months	6 months	9 months	12 months
Round the head (cm)	35.5±0.8	37.8±0.54	42.1±0.7	43.8±0.74	45.7±0.74	47±0.9
Weight (kg)	3328±3.25	4467±3.48	7016±3.53	8118±3.57	9285±3	9646±2
Height (cm)	50±1.4	53.7±1.3	62.9±1.2	67.1±1.5	71.6±1.2	75.1±1.3
Weight to height ratio (%)	42.1±28.1	51.6±28.7	63.6±19.4	70.3±17.4	74±12.3	76.5±13.6

Table 3: Weight, height, round of the head and weight to height ratio in infants with congenital hypothyroidism by sex.

Variables	Sex	Birth time	1 month	4 months	6 months	9 months	12 months
Round the head (cm)	Girl	43.3	45.2	48.6	58.2	59.8	64.4
	Boy	55.6	61.9	67.2	74.3	80.1	80.3
	P value	0.11	0.005	0.001	0.001	0.001	0.001
Weight (kg)	Girl	40.6	31	31.4	34.8	37.8	41.5
	Boy	70.1	59.1	64.5	69.7	69.8	65.6
	P value	0.001	0.001	0.001	0.001	0.001	0.001
Height (cm)	Girl	67.3	63.8	65.9	72.5	71.6	76.7
	Boy	83	81.8	77	77.8	81.1	83.5
	P value	0.002	0.001	0.055	0.22	0.092	0.2
Weight to height ratio (%)	Girl	49.5	59	65.3	73.4	69.7	72.1
	Boy	35.5	44.9	62.1	67.5	77.8	80.4
	P value	0.12	0.12	0.6	0.29	0.038	0.053

The average height and weight of newborns with hypothyroidism at birth were 49.01±3.05 and 3.192±0.473 respectively. The average of the first TSH among 180 neonates with hypothyroidism was 29.7±26.7 µIU/ml and its level was 30.6±28 µIU/ml in the second time. The median of TSH in these patients was at the first and second times of 16 and 21. Of the 180 infants, 117 (60.9%) had positive familial history (Table 1). The incidence of transient and persistent hypothyroidism in this study was 1 to 916 and the definitive permanent hypothyroidism prevalence was 1 to 4000. Of the 40 infants with permanent hypothyroidism, 21 (52.5%) were female and the mean age of treatment in these patients was 18.45±6.22 days. 16 (40%) infants were born from non-family marriage. 13 newborn (32.5%) had a positive familial history of thyroid disease. In newborns with permanent hypothyroidism the average of TSH levels in the first and second times was 37.15 and 31.56 µIU/ml, respectively. The average of T4 and T3RU levels in these infants was 16.04 µg/dl and 4.74 mg/dl, respectively. In these infants, height increase, weight to height ratio, Round the head (both centimeters and percentile) were statistically significant during the studied times (at birth time, 1,4,6,9 and 12 months late) (Table 2).

Weight, height, round the head and percentile of weight to height by sex were also investigated at different times. The results showed that the percentile of weight in the boys significantly was more than girls at times 1, 4, 6, 9 and 12 months of age. The percentile of weight in boys in all cases was significantly higher than girls. A percentile around the head in boys at birth time and one month late was significantly more than girls. In the study of percentiles of weight to height in boys, only 9 and 12 months were more than girls and in other cases it was less than girls and significant difference was observed at 9 month of age. There was no significant difference between the sex and level of TSH. The level of T4 at birth time in boys with 4.91 was significantly lower than girls with 10.26 (p=0.044). There was no significant difference at the level of T3RU between girls and boys (Table 3).

DISCUSSION

In this study, the recall rate of infants was 5600 infants and the hypothyroidism (permanent and transient) was 180 infants (0.03%, 1:916 live births) and permanent hypothyroidism was 0.7% (1:4000 live births).

In studies conducted elsewhere, the prevalence of hypothyroidism varied from 0.7 per 1,000 live births to 7.1 per 1,000 and in the present study, the prevalence of hypothyroidism with 39 per 1000 was higher than other studies.[12-16]

According to research in the world, the prevalence of congenital hypothyroidism varied from 0.14 per 1,000 live births in Japan to 14.7 per 1,000 infants in Nigeria which lower than the present study.[7,17,18]

The causes of the different prevalence of the disease in different parts of the world can be due to the different contraceptive criteria for the diagnosis of hypothyroidism, use of T4 or TSH to screen, iodine

deficiency in some parts of the world, the percentage of different marriages and ethnic and racial differences.[19-25]

In this study, the rate of recall was 5600 cases or 35 cases per 1000 (3.5%) infants. In the Siami's study (25), the recall rate was 6.1%. In other countries, the sampling rate of the heel was 0.3-0.1% and in the umbilical cord sampling was 0.16-1.05%.[15,28]

The rates of recall in other countries are usually different with the usual screening methods between 3-5 days after birth from 0.16% in the Philippines and 2.3% in Turkey to 3.3% in Estonia.[23,26,27] One of the reason for the high recall rate in this study is that due to the importance of illness and impose high economic cost, the TSH>5 was considered as the basis for recall that in other studies, the usual limit for screening of hypothyroidism is TSH>10 mu/L.[16]

In this study, 56.7% of infants with permanent and transient hypothyroidism and 52.5% of infants with permanent hypothyroidism were girl. In terms of low prevalence of hypothyroidism in Saudi Arabia female to male ratio 1.8 to 1, in Estonia 4 to 1 and in China 3 to 2, and in other studies in Mazandaran, as well as study by Siami and colleagues, this ratio was almost equal. [15,24,25,27]

Among newborns with permanent and transient hyperthyroidism 39.1% and 32.5% of newborns with permanent hyperthyroidism had a positive history of disease. The relative familial relation in Ordoukhani study was 68.2%, which was higher than the present study and diet and environmental factors are involved in this, which requires more studies in the future. [13] Based on results of more studies, early detection and therapy with thyroxin potentially prevent developmental disorders of the nervous system.[28] In few studies, early treatment has also been effective in improving the intelligence of these patients but in two other studies this communication was not significant.[29,30]

In this study the average birth weight of babies was 3.328 kg. After assessing the percentile weight of newborns, it was observed that with increasing age, the weight percentile of newborns also increased and all babies at all stages of their monitoring were above the percentile of 3%. However in a study conducted in New York in 2000-2003, the highest number of neonates with a hypothyroidism weighing less than 2500 gr and at a weight above 2500 gr the prevalence of hypothyroidism had been low.[30] Several studies have concluded that with the onset of timely treatment, the weight of neonates is close to normal.[31] In a study on 2341 children with congenital hypothyroidism in Japan in 2007, the growth of these children in case of onset of treatment between standard deviation -2 and +2 was reported.

After review the height of the infants, it was observed that with increasing age at first one month of age, the percentile age decreased and then the percentile height increased which this increase has raised between 9-12 months. In the Feyzi and et al study, the height of children at age of 5 reached to normal values. Although some studies did not observe any differences in the growth rates of children in the affected population, some reported natural growth at age 3 and others at age 6.[31-33] Moschini and et al reported normal growth height at the age of 6 in children with an average age of treatment beginning at 33 days.[34]

CONCLUSION

Based on the evidence from this study, congenital hypothyroidism has a high prevalence in Ardabil. The average starting age of treatment after diagnosis and its distance from the birth is at an acceptable distance. Comparing the results of this study with other studies in other countries suggests the proper efficacy of congenital hypothyroidism screening in Ardabil's health system.

In future studies, consideration should be given to other environmental factors especially during pregnancy which affect the functioning of the mother's thyroid and consequently the baby. Because of positive familial history in one quarter of patients, we can noted the role of other environmental factors in addition to genetic factors in the high incidence of hypothyroidism in the Ardabil area. Increasing the length of follow-up in infants with hypothyroidism until adolescence can better determine the quality of treatment in the neonatal period by assessing their IQ and their educational performance and suggesting future studies in this regard.

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