Evaluation of Frequency of Congenital Hypothyroidism and its Risk Factors in Newborns in Kohgiluyeh County (2013-2016)

Elahe Piraee¹, Habibollah Azarbakhsh², Zahra Shakolohi³, Maysam Abshenas⁴, Mohammad Hossein Ravaee⁵ and Sayed Hasan Faghihi⁶*

¹ Master of Epidemiology, Social Determinants of Health Research Center, Yasuj University of Medical Sciences, Yasuj, Iran
² MSc of Epidemiology, Ahvaz University of Medical Sciences, Ahvaz, Iran.
³ Master of Nursing, Shiraz University of Medical Sciences, Shiraz, Iran.
⁴ Public Health Expert, Golestan University of Medical Sciences, Golestan, Iran.
⁵ Public Health Expert, Yasuj University of Medical Sciences, Yasuj, Iran.
⁶ Graduate Student of Epidemiology, Department of Statistics and Epidemiology, School of Public Health, Isfahan University of Medical Sciences, Isfahan, Iran
*Corresponding author: Sayed Hasan Faghihi, sayedhasanfaghihi2016@yahoo.com

Abstract:
Introduction: Congenital hypothyroidism is one of the most common endocrine diseases and is one of the most important causes of mental retardation. The present study was conducted to determine the prevalence of hypothyroidism and its effective factors in Kohgiluyeh County from 2013 to 2016.

Materials and Methods: This case-control study was performed on newborns born in Kohgiluyeh County who participated in the congenital hypothyroid screening from March 2013 to February 2016. Neonates with TSH (Thyroid-Stimulating Hormone) were healed more than or equal to 5. Then, their serum TSH level was measured. Newborns with a TSH level greater than or equal to 10 µu/L were considered as congenital hypothyroidism. For each patient, three healthy children were selected as controls. SPSS software was used to analyze the data.

Results: The incidence of disease was 5.56 in 1000 live births during these four years, of which 1 case was diagnosed in 180 live births. Boys were 20.6% more likely to have hypothyroidism than girls. There was no significant relationship between the type of delivery and the incidence of hypothyroidism (P> 0.05). Also, there was a significant relationship between the history of hypothyroidism in the family and hypothyroidism (P = 0.001).

Conclusion: The prevalence of congenital hypothyroidism in Kohgiluyeh County city is more than national and global statistics, which has concerns (1: 180 live births).

Key words: Congenital hypothyroidism, screening, neonates
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Revista Publicando, 5 No 16. (2). 2018, 387-394. ISSN 1390-9304

Introduction
Congenital Hypothyroidism (CH) is a prerequisite for mental retardation in the world (1). The evaluation of thyroid activity in newborns is very important, so that neonates with hypothyroidism often have normal appearance and clinical symptoms at birth are low and non-specific. Therefore, the child has irreparable complications if the diagnosis is based on clinical symptoms only (2-4). The known etiologies of transient hypothyroidism include iodine deficiency and high levels of iodine in infants, the use of drugs affecting thyroid function and goiterrogens by mothers in the perinatal period, and the transfer of antibodies to the neonatal thyrotropin receptor blocker antibodies (6,5 ) Recently, rare cases of gene mutations associated with hypothyroidism have also been reported (7). In some cases, the cause of hypothyroidism remains unknown (6).
That's why it's been paying a lot of attention over the last three decades. Today, in many countries, thyroid screening tests are in place at birth (8). The screening program for infants has been implemented in the United States since the mid-1970s (9). Following the elimination of iodine deficiency in Iran, congenital hypothyroidism screening began in Tehran from March 1997 (10).
The prevalence of CH in the world is estimated to be 4.7 per 1,000 babies in Nigeria (8) to 14.0 per 1,000 babies in Japan (11). Is different CH in the provinces of Iran also has a variable prevalence (12). Neonatal screening for CH diagnosis is cost effective (5) and in the last 40 years has been able to prevent mental disorders in many patients and reduce the socioeconomic burden of the disease (13). Cost estimates are similar in screening programs, and roughly between $ 0.70 and $ 1.60 per screening for each infant. The ratio of profits to costs varies from 7 to 11 to 1 in some developed countries (14) and in Iran it is 15 to 1 (15). The present study was conducted to determine the prevalence of hypothyroidism in Kohgiluyeh County from 2013 to 2016.

Materials and Methods
A case-wise study was conducted to determine the prevalence of hypothyroidism and its effective factors in Kohgiluyeh County during 2013-2016. The present study was conducted from March 2013 to the end of March 2016 on 13675 newborns born in Kohgiluyeh, who participated in the congenital hypothyroidism screening program. The coverage of neonatal screening coverage in Kohgiluyeh County is approximately 100%. All infants diagnosed and confirmed as congenital hypothyroidism were included in the study. For each case, three healthy children (control) matched for birth year and place of birth were selected. . To implement the plan, the Ethics Committee of the Vice-Chancellor for Research in Yasuj University of Medical Sciences was originally assigned a code of ethics. Based on the country protocol, all neonates born on 3-5 days after the birth of the heel and foot samples are taken on a filter paper for screening test. This work was carried out with Lanst by trained samplers in a country design in urban and rural health centers, and health and health houses in the city. Babies with TSH levels above 5 have been referred for confirmation of diagnosis by TSH and T / 4 tests, and clinical examinations. Generally, two TSH, T4 tests on filter paper are used to screen for hypothyroidism. The sensitivity of both tests is identical in identifying the disease, but some believe that the sensitivity of the initial TSH test is higher. In addition, the TSH concentration
remains constant longer than the T4 on the filter paper. For the same reason, TSH measurement is the primary screening test for this program.

Premature, low weight, overweight 4500 grams, twin and colon, neonates who have had hospital records for any reason, were re-tested after two weeks. Infants who in the second stage (recall) have a TSH higher than (10 μ/L) and T / 4 less than (6.5 mg / dl) as a neonate with congenital hypothyroidism treated with levothyroxine. Then, at 3 to 5 years of age, to determine the transient or continuous CH with discontinuation of the drug, the levels of TSH were re-measured and in the transient type no further treatment with levothyroxine was required (26, 27).

**Data analysis**

Data were analyzed by SPSS software version 21. Data were analyzed using central indexes and dispersion tables and charts. Quantitative and qualitative data analysis was performed using chi-square test and logistic regression. The significance level of this study, similar to other studies, was considered to be 0.05. Quantitative data were analyzed using Kolmogorov-Smirnov test for normalization.

**Findings**

The total of all screened neonates from 2013 to the end of 2016 in Kohgiluyeh County was 13675 infants, approximately 100% of neonates born in Kohgiluyeh. 48.46% of screened newborns were 51.54% of boys. The number of patients was 78, and the incidence of the disease was 5.56 per thousand live births during these four years. That is 1: 180 live births per year. The incidence of congenital hypothyroidism in Kohgiluyeh County students over a period of 4 years (2013 to 2016) was generally 1 in 180 live births (incidence of hypothyroidism was 5.56 cases in 1000 live births), Which was 2013 in live births (5/05 in 1,000 or 1: 200 live births) in 2014 (6/94 in 1,000 live births or 1: 144 in live births) in 2015 (4.88 in 1000 live births or 1: 205 live birth), and in 2016 (5.17 per 1,000 live births and 1: 193 live births). The results of births born annually are listed in Table 1.

**Table 1: Frequency of Born and Screened Neonates in Kohgiluyeh County from 2013 to 2016**

<table>
<thead>
<tr>
<th>Variable name</th>
<th>The number of neonates screened</th>
<th>Number of girls screened</th>
<th>Number of sons screened</th>
<th>Coverage percentage</th>
<th>Number of patients detected</th>
<th>Percent</th>
<th>Number of patients detected</th>
<th>Percent</th>
<th>Number of patients detected</th>
<th>Percent</th>
<th>Number of patients detected</th>
<th>Percent</th>
<th>Number of patients detected</th>
<th>Percent</th>
<th>Number of patients detected</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>3764</td>
<td>1811</td>
<td>1953</td>
<td>100</td>
<td>3530</td>
<td>93.7</td>
<td>8</td>
<td>234</td>
<td>19</td>
<td>5.04</td>
<td>63</td>
<td>37</td>
<td>144</td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>3747</td>
<td>1834</td>
<td>1913</td>
<td>100</td>
<td>3589</td>
<td>95.7</td>
<td>8</td>
<td>158</td>
<td>26</td>
<td>6.94</td>
<td>57</td>
<td>56</td>
<td>144</td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>3072</td>
<td>516+</td>
<td>1556</td>
<td>100</td>
<td>2913</td>
<td>94.8</td>
<td>2</td>
<td>156</td>
<td>15</td>
<td>4.88</td>
<td>56</td>
<td>44</td>
<td>144</td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>3092</td>
<td>1484</td>
<td>1608</td>
<td>100</td>
<td>2937</td>
<td>95</td>
<td></td>
<td>155</td>
<td>18</td>
<td>5.17</td>
<td>56.25</td>
<td>43.75</td>
<td>144</td>
<td>37</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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Approximately 95% of the infants have been screened for congenital hypothyroidism 3-5 days after birth. In total, 60.3% (47 cases) of males and 39.7% (31 cases) of the patients were diagnosed. The mean first-time TSH in the newborns was 11.6 ± 5.2. Birth weight and birth weight in neonates with congenital hypothyroidism were 3024.9 ± 609.1, 49.18 ± 3.4, respectively. The mean of birth weight in healthy infants (control group) was 3258 ± 516.5 and 47.6 ± 2.4, respectively. In relation to the parents' relative ratio, it was found that 40 (51.3%) of neonates with congenital hypothyroidism were their non-familial parents, and 26.9% in the case group of their newborns had a grade-3 familial relationship.

Table 2: The mean and standard deviation of the variables studied in the study of the profile of newborns with hypothyroid disease in Kohgiluyeh County during 2013-2016

<table>
<thead>
<tr>
<th>Variable name</th>
<th>Number</th>
<th>Mean (Standard deviation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother's age (years)</td>
<td>78</td>
<td>(5.9) 29.99</td>
</tr>
<tr>
<td>Gestational age of the mother (week)</td>
<td>78</td>
<td>(1.6) 38.4</td>
</tr>
<tr>
<td>Infant birth weight (g)</td>
<td>78</td>
<td>(609.12) 3024.9</td>
</tr>
<tr>
<td>Infant Height (cm)</td>
<td>78</td>
<td>(3.4) 49.18</td>
</tr>
<tr>
<td>TSH levels are the first turn</td>
<td>78</td>
<td>(5.21) 11.63</td>
</tr>
<tr>
<td>Second stage TSH</td>
<td>66</td>
<td>(4.15) 13.5</td>
</tr>
<tr>
<td>Venous TSH levels</td>
<td>42</td>
<td>(3.34) 29.5</td>
</tr>
<tr>
<td>T4 venous level</td>
<td></td>
<td>(3.73) 7.33</td>
</tr>
</tbody>
</table>

On this basis, it was found that 63 (94.04%) of infants with congenital hypothyroidism due to TSH levels ranged from 5 to 9.9 for re-sampling. According to the findings of this study, 60.3% of the patients were male and 39.7% were female. The findings of the study showed that 67.9% of the patients in the newborns and 67.1% of deliveries were in the healthy newborns of the cesarean section. However, the incidence of congenital hypothyroidism in neonates born with cesarean section was 1.01 times more than infants they were born with normal birth, but there was no significant relationship between the type of delivery and the incidence of hypothyroidism (P > 0.05). Also, there was a significant relationship between the history of hypothyroidism in the family and the hypothyroidism (P = 0.001). The results of this study showed that the chances of illness in neonates with a history of disease in the family were more
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than those with a history There is no illness in the family, the chance of the disease is 8.5 times (0.001).

Discuss
In this study, 13675 newborns were screened for congenital hypothyroidism in 3-5 years after birth in the years 2013 to 2016, with TSH≥5 in the first sample for recall sampling. Approximately 10% of newborns were called each year for re-sampling. According to the results of this study, the incidence of congenital hypothyroidism was reported in Kohgiluyeh County during 4 years 1 in 180 live births (incidence of hypothyroidism was 5.56 cases in 1000 live births), which was 2013 (5.05 per thousand) Or 1: 200 live births) in 2014 (6.94 per 1000 live births or 1: 144 live births) in 2015 (4.88 per 1,000 live births or 1: 205 live births) and in 2016 (5.17 per 1,000 live births and 1: 193 live births). From the onset of screening for infants, the incidence of congenital hypothyroidism was reported based on clinical manifestations of 1: 7000 to 1: 1000 live births.

With the onset and progression in screening tests, the incidence rate was 1: 3000 to 1: 4000 (17, 16). (2, 17 Mashhad), with the experience gained from national and regional screening programs from different parts of the world, it was found that the incidence of the disease varies according to the geographical area, ethnicity, and race. A report from the French Neonatal Screening Program during a 20-year period provided a 1: 10000 live birth rate to the permanent birth control (9, 16). While Greece's screening report, during a 11-year period, offered a hypothermic ratio of 1: 800 (16). The same study reported the incidence of hypothyroidism in the United States from 1: 4094 in 1987 to 1: 2372 in 2002. The cause of an increase in incidence is unknown, but may be due to a change in the testing strategy. With the increased sensitivity and precision of the TSH screening method, in the United States and other screening programs around the world, the initial T4 measurement method, followed by TSH, may change to the initial measurement of TSH. In this case, most infants are diagnosed with milder illness. Several screening programs report a higher incidence of the disease in Asia (1: 1016 and Spain, 1: 1559), with a lower incidence in American black than whites (9).

In a study conducted by Erdokhani et al. In Tehran, the prevalence of congenital labor in neonates was reported in 914 live births (10). In a study by Karami Zadeh and Amir Hakimi in Shiraz, the incidence of this disease was reported in 1 in 1433 cases (18). In recent years, the incidence of congenital hypothyroidism in Isfahan was one in 342 live births and In 2002, one in 333 live births in Kerman 1 in 1,000 cases 2009, in Qazvin 1 in 446 cases and in Borujerd 1 in 397 cases (19-21). These figures indicate that the prevalence of congenital hypothyroidism in Kohgiluyeh County is much higher than in the world average and in Iran. The factors contributing to the high incidence of congenital hypothyroidism in Kohgiluyeh County include iodine deficiency in the region, low iodine intake in salts, ethnic-demographic differences, increased public awareness, follow up of health authorities and families. To participate in screening and environmental factors, inheritance and family marriage.

In the present study, boys were 20% more likely to have congenital hypothyroidism than girls, but there was no significant relationship between gender and disease. This study was similar to a study conducted in Isfahan in 2002-2003. Of these, 43.4% of the neonates had a female hypothyroidism and 56.4% of them were boys (22). In Yazd, the female sex / male sex ratio was reported to be 1.25 / 1 and in Isfahan was 1.54 / 1. In our study, there was a slight increase
in the incidence of malaria in the male population, and is consistent with recent studies in Yazd, Esfahan, and East Azerbaijan (12, 23, and 24).

In 21.8% of the infants with congenital hypothyroidism, thyroid disease was observed in the family members. The results of our study are consistent with the results of Medda et al. (25). In the present study, no significant relationship was found between the incidence of MAD and the mother's birth.

**Conclusion**

Deferring diagnosis and treatment of congenital hypothyroidism, even for 3 months after birth, leads to loss of intelligence. However, the diagnosis and treatment of this disease is very easy. Therefore, in view of the high prevalence of congenital hypothyroidism in Kohgiluyeh, informing people and health care staff to encourage parents to participate in screening for congenital hypothyroidism, especially in women's routine care and increasing the coverage of this plan is necessary. Also, due to high incidence and high recurrence in this city and the probability of iodine deficiency or high in the region, supplementary studies are recommended to evaluate the iodine levels in mothers and newborns.

**Acknowledgment**

This research project was approved by the research council of Yasuj University of Medical Sciences and sponsored by the university. We sincerely congratulate ourselves on the sincerity of the cooperation of experts in the field of health centers and also the management team of Kohgiluyeh County who helped us with this research.

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Revista Publicando, 5 No 16. (2). 2018, 387-394. ISSN 1390-9304


Received 24/08/2018
Approved 28/09/2018
Evaluation of Frequency of Congenital Hypothyroidism and its Risk Factors in Newborns in Kohgiluyeh County (2013-2016)

Revista Publicando, 5 No 16. (2). 2018, 387-394. ISSN 1390-9304
