Volume: 3, Issue: 2, May 2018, Pages: 253-258, DOI: http://dx.doi.org/10.19082/ah253

FREQUENCY OF CONGENITAL HYPOTHYROIDISM IN HORMOZGAN PROVINCE, IRAN

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TYPE OF ARTICLE: ORIGINAL

ABSTRACT

Background: Congenital hypothyroidism, defined as thyroid hormone deficiency at birth, is one of the most common preventable causes of mental retardation.

Methods: This study was a cross sectional investigation conducted prospectively on 45,799 live births from September 2010 to February 2012 in the Hormozgan province, Iran, who participated in congenital hypothyroidism screening. In accordance with national protocol, blood samples were taken from the heels of the newborns 3-7 days after their birth. Neonatal TSH values less than 5 mIU / L were considered as normal; TSH values greater than or equal to 5 mIU/L were considered as suspicious, and an immediate report was made to the Focal Point of the newborn's birth place. Descriptive statistics including mean, frequency and percentage were used to present the results. SPSS version 20 and t-test was used for comparison of continuous quantitative variables (age and weight) and Chi-Square test was used to determine the qualitative relationship between variables.w

Results: Out of 45,799 infants in the initial study, Blood TSH was ≥5 mIU/L in 1,241 infants (2.7%). Of these 1,241 infants, 1,159 cases (93.3%) had TSH between 5-9.9 mIU/L, 39 infants (3.1%) between 10-19.9 mIU/L, and 43 infants (3.46%) ≥20 mIU/L. The incidence of congenital hypothyroidism in the province was estimated at 1/715 live births. The mean TSH of 64 infants suffering from congenital hypothyroidism was reported 36.8±34 mIU/L (10-100). The mean age of the infants at the time of admission for second sampling was 7.5±6.5 (3-30) days.

Conclusion: In view of the high incidence of congenital hypothyroidism in Hormozgan province, several times more prevalent than many areas of the world, the continuation and strengthening of the neonatal screening program appears indispensable.

KEYWORDS: Hypothyroidism, Congenital, Iran

1. INTRODUCTION

Newborn screening (NBS) is a public health program where all newborn babies in a demographic area are screened for treatable diseases in early life. The diseases selected for NBS are those for which early treatment and diagnosis will prevent mortality or significant irreversible morbidity (1). Congenital hypothyroidism, defined as thyroid hormone deficiency at birth (2), is one of the most common preventable causes of mental retardation (3). It is most frequently due to thyroid dysgenesis (80-85%) or dyshormonogenesis (2, 4). The patients suffering with this disease are usually asymptomatic at birth but must be suspected in case of a history of autoimmune thyroid disease in the mother, lack of iodine in the mother's diet, maternal treatment with radioactive iodine during pregnancy or if the child presents with lethargy, jaundice longer than 3 weeks, hiatal hernia, macroglossia, cold and dry skin (2). Overall, only 10% of babies are identified within 1 month, 35% within 3 months, 70% within 1 year and 100% within 3-4 years on the basis of clinical symptoms (2, 5). Most infants with hypothyroidism will have normal Intelligence Quotient (IQ), and normal brain development when treated in the newborn period, whilst failure to start treatment at an early stage can lead to severe mental deficiency needing special care (6). Prior to the implementation of congenital hypothyroidism screening programs, the incidence of congenital hypothyroidism, as diagnosed based on clinical symptoms, was reported to be 1/7000 to 1/10000 which increased to a range of 1/3000 to 1/4000 after the

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Received: December 30, 2016, Accepted: XXX, Published: May 2018
iThenticate screening: September 12, 2017, English editing: February 14, 2018, Quality control: March 23, 2018
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implementation of the screening program first performed in 1970s by Dussault and Laberge (7). Recent studies show that the rate has increased in the US from 1/3985 in 1987 to 1/2274 in 2002 (8). The incidence of congenital hypothyroidism was higher in Asian and Hispanic races compared to other races, in mothers aged over 39 years compared to those aged less than 20 years, in cases of premature birth to term birth, and in girls compared to boys (2). The first congenital hypothyroidism screening program in Iran was conducted by Azizi et al in 1987, established more extensively in 2004 and several studies of incidence have been conducted in various parts of the country (3). Notwithstanding, Hormozgan was the last province to join the country's screening program in the autumn of 2007. In recent studies in the country, Hormozgan province had a screening coverage of less than 50%, which is considered a poor performance (9). In view of the importance of this issue and lack of sufficient information available in the Hormozgan province and its counties, this study was conducted to investigate the frequency of hypothyroidism in the province.

2. MATERIALS AND METHODS

This study is a cross sectional investigation conducted prospectively on 45,799 live births from September 2010 to February 2012 in the Hormozgan province who participated in congenital hypothyroidism screening. In accordance with national protocol, heel blood samples were taken from the newborns 3-7 days after their birth by trained health professionals in health centers across the province. For sampling, the outside of the heel was pierced with a lancet and about 5-4 drops of blood were gathered on a Guthrie paper (Filter paper S&S 903). Then, the filter paper was placed horizontally to dry at 15-25 °C room temperature for 2-3 minutes. Dried samples were placed in an envelope and sent to disease units and, on a daily basis, to the reference laboratory of the province (Lab # 5 of Bandar Abbas). TSH levels of the dried samples were measured through ELISA method using Kimia PazhuhanTM kit. Neonatal TSH values less than 5 mIU/L were considered as normal; TSH values greater than or equal to 5 mIU/L were considered as suspicious and immediate report was made to the Focal Point of the baby's birth place (in accordance with the guidelines of the Ministry of Health, the cut-off point for TSH was considered greater or equal to 4 for babies who did not visit at the appointed time and their first visit was after the 7 days). Venous blood samples were taken from the cubital vein of neonates with TSH=5-9.9 mIU/L at four weeks of age, those with TSH=10-19.9 mIU/L at 2-3 weeks, and those with TSH≥ 20 mIU/L immediately after birth to determine the concentration of TSH and T4. They were tested using Electrochemiluminescence method with a HITACHI set model Cobas e411. Based on the test results, the neonates with TSH≥ 10 mIU/ml or T4 <6.5 µg/dl were considered as suffering from congenital hypothyroidism and referred to a pediatrician for assessment and treatment. Treatment was started immediately to babies with TSH≥ 20 mIU/L. Once hypothyroidism was diagnosed, forms were filled out at the city health center where the following information was recorded through an interview: gender, weight, date of birth, type of delivery (using infant health records), parental intermarriage (consanguinity), type of salt used every day, and history of hypothyroidism or hyperthyroidism in the mother. Data were collected from different cities of the province. Descriptive statistics including mean, frequency and percentage were used to present the results. SPSS version 20 and T-Test was used for comparison of continuous quantitative variables (age and weight) and Chi-Square test was used to determine the qualitative relationship between variables. P value <0.05 was considered statistically significant.

3. RESULTS

The coverage of screening programs in the province was estimated at 93.4% from September 2010 to February 2012. On this basis, 45,799 infants were studied in 11 cities of the province. Out of this number in the initial study, Blood TSH was ≥5 mIU/L in 1241 infants (2.7%). Of these 1,241 infants, 1159 cases (93.3%) had TSH between 5-9.9 mIU/L, 39 infants (3.1%) between 10-19.9 mIU/L, and 43 infants (3.46%) ≥20 mIU/L. All 1,241 infants who had Blood TSH ≥5 mIU/L were recalled. After carrying out tests on the infants' serum, infants whose serum TSH ≥10 mIU/ml or T4<6.5 µg/dl (n=64) were treated after the diagnosis of congenital hypothyroidism. In this regard, the incidence of congenital hypothyroidism in the province was estimated at 1/715 live births. The mean TSH of 64 infants suffering from congenital hypothyroidism was reported as 36.8±34 mIU/L (10-100). The mean age of the infants at the time of admission for the second sampling was 7.5±6.5 (3-30) days. Age at this admission was 3-7 days in 51 cases (79.7%) and more than 7 days in 13 infants (20.3%). Out of 64 infants suffering from congenital hypothyroidism, 35 cases (54.7%) were males and 29 (45.3%) were female (p=0.53). The average height of the 64 hypothyroid infants was 48.7±3.3 cm (39-58 cm) (p=0.14) and the average weight was 2935±656 g (1220-4500 g) (p=0.39). Height and weight of girls and boys with congenital hypothyroidism was similar. Out of the mothers of 64 infants with congenital hypothyroidism, only 4 mothers (6.3%) had a history of hypothyroidism; all had been treated with levothyroxine. None of the mothers had a history of hyperthyroidism. All (100%) of the mothers were taking

iodized salt. The frequency of congenital hypothyroidism in the east and the west of the province were compared: the disease was 3 times as frequent in the west as the east of the province. Bastak (1/233) and Bandar Khamir (1/271) had the greatest frequency while Minab (1/1818) had the lowest. The geographical difference in the incidence of congenital hypothyroidism was statistically significant (p=0.004). The average age for beginning of treatment was 28.5±13.3 days (varying from 9 to 70 days). In 28 infants (43%), treatment was begun after 28 days of age (Figure 1).

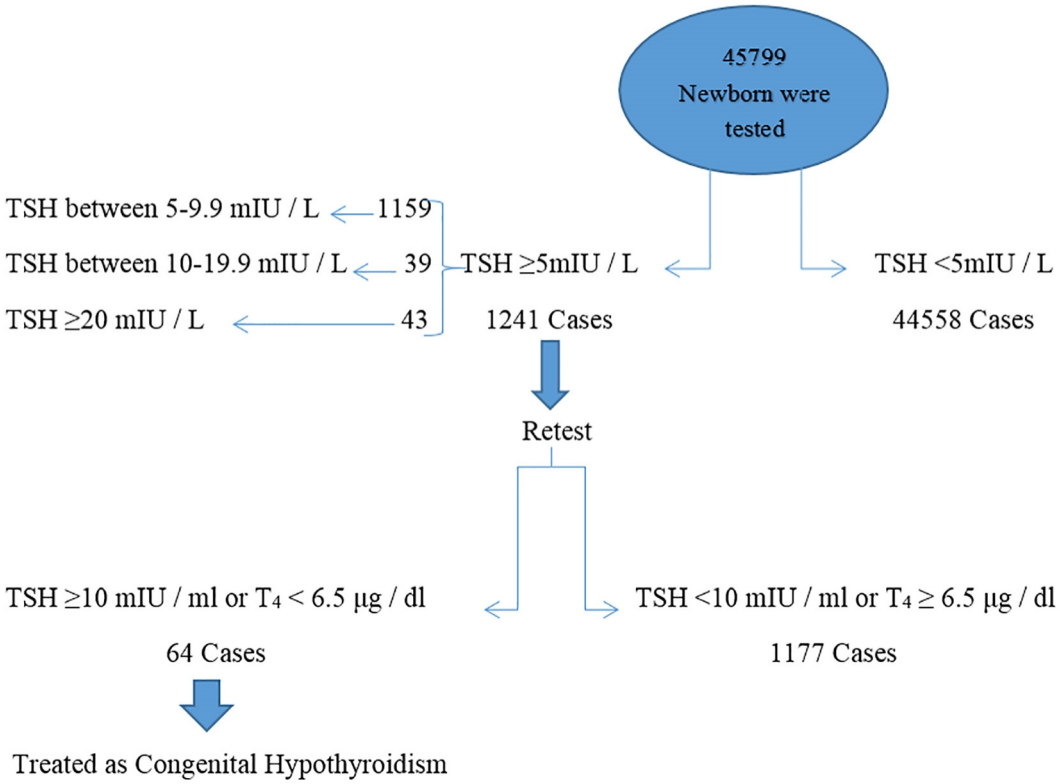

Figure 1. Hypothyroidism screening results

4. DISCUSSION

The incidence of congenital hypothyroidism has been estimated at 1/3000 and 1/4000 live births in the countries employing a screening program. Regarding the frequency (1/715 live births) in this study, the rate in Hormozgan province is 4-6 times greater than reported above. The incidence of congenital hypothyroidism varies from 1/781 in Pakistan (10), 1/1130 in India (11), 1/1823 in Lebanon (12), 1/2736 in Turkey (13) to 1/8000 in north east Thailand (14) and is 1/10000 for live births in African-Americans (15). In a study in the period between 1987 and 2008 (first period: from 1987 to 1998 and the second period: 1999-2008) was performed on newborn babies in Italy, of the 10,190,000 babies screened, 4,195 were reevaluated and 3,721 were diagnosed with permanent congenital hypothyroidism. The incidence was reported as 1/1940 for live births in that study (16). In another study conducted in England in 1982, the incidence of congenital hypothyroidism was reported as 1/3937 and higher in babies of Asian mothers compared to other races (17). The higher incidence in the Asian race was also observed in New York (1/1016 live births) (18). Ordookhani et al. reported the incidence of congenital hypothyroidism as 1/914 live births in Tehran (19) and Karamizadeh et al., as 1/1465 in Shiraz (20). According to the studies conducted in other cities in recent years, the incidence of congenital hypothyroidism was 1/1000 in Kerman (21), 1/466 in Qazvin (22), 1/397 in Borujerd (23), and in Isfahan 1/342 in 2002 and 1/333 live births in 2009 (Table 1) (24). According to our results, the incidence of congenital hypothyroidism in Hormozgan province is much higher than the global average, and is in average ranking compared to Iran's. The reasons cited for the differences in the incidence of congenital hypothyroidism in different areas of the world are: different criteria for diagnosis of hypothyroidism, the contribution of iodine deficiency in some parts of the world, especially for the transient type of hypothyroidism, and genetic differences (25, 26). In the present study, out of 64 infants suffering from congenital hypothyroidism, the ratio of boys to girls was 1.2 to 1. In east Azerbaijan the incidence ratio girls/boys was 1.0 to 1.45 (18). According to

the studies conducted in Saudi Arabia, Estonia and Japan, the disease was more frequent in girls than boys and the ratio was 1.8 to 1 (27), 4 to 1 (28) and 3 to 2 (29), respectively. In the present study, 2.7% calls were observed. The percentage was 3.3 in South Khorasan (30) and it was reported to vary from 0.16% in the Philippines (31) to 3.2% in Turkey (13) and 3.3% in Estonia (28) where the common method of screening had been done between 3-5 days after birth. The rate of calls in Iran and Hormozgan province as compared to that in Western countries, where the call quorum was higher and the call rate was lower than that of Iran, indicates that differences in the quorum can play an important role in the rate. It seems that re-sampling from the feet of infants with TSH between 5-9.9 days can reduce the number of calls. Among the infants who had a positive screening test, 1,159 patients had TSH equal to 5-9.9 mIU/L out of whom 38 infants (3.2%) were diagnosed as hypothyroid in the definitive diagnostic tests. Out of the 39 infants who had TSH equal to 10-19.9 mIU/L, 8 cases (20%) and also out of 43 infants with TSH greater than 20 mIU/L, 18 cases (41.8%) were hypothyroid. These statistics are consistent with several studies conducted in Iran. According to a study conducted in Arak, 36 patients (41.8%) had TSH equal to 5-9.9 mIU/L, 19 patients (22.9%) had TSH equal to 10-19.9, and 26 cases (30.33%) had TSH greater than 20 mIU/L (32). In another study in the South Khorasan, 32 infants (45%) had TSH equal to 5-9.9 mIU/L, 14 infants (20%) had TSH equal to 10-19.9, and 25 cases (35%) had TSH greater than 20 mIU/L (30). In the current study, congenital hypothyroidism was rejected in 96.81% of neonates with TSH = 5-9.9 mIU/L but more than half of our patients had TSH equal to 5-9.9 mIU/L. Therefore, the number of calls greater than or equal to 5 for TSH seems logical, and the call percentage can be reduced in this group by replicating heel screening test from infants with TSH = 5-9.9 mIU/L. In this study, the average age for beginning treatment was 28.5±13.3 days (varying from 9 to 70 days). In 28 cases (43%), the treatment was begun at an age of more than 4 weeks. In a similar study conducted in Mazandaran in 2007-8, the average age for beginning treatment was 25 days (33). In a pilot study in Turkey, the average age for beginning treatment was reported as 23 days (13). Also, in a study performed in Italy, the average age for beginning treatment was 23 days and 19 days in the first and second period, respectively (16). In, the national screening program, venous sampling is done at an age of 2 or 3 weeks to confirm the diagnosis in infants with TSH=10-19.9. The same is done at the age of 4 weeks in the infants with TSH=5-9.9 mIU/L. Although the testing carried out according to these instructions reduces the number of transient hypothyroidism cases, it delays the start of treatment.

Table 1. Comparison of hypothyroidism incidence based on first step of screening

Province	TSH Level			
	TSH = 5-9.9 mIU/L	TSH = 10-19.9 mIU/L	TSH > 20 mIU/L	Total
This study (Hormozgan)	38 (59.38%)	8 (12.5%)	18 (28.12%)	64 (100%)
Arak	36 (41.8%)	19 (22.9%)	26 (30.33%)	81 (100%)
South Khorasan	32 (45%)	14 (20%)	25 (35%)	71 (100%)

5. CONCLUSIONS

In view of the high incidence of congenital hypothyroidism in Hormozgan province being several times larger than many areas of the world, the continuation and strengthening of the neonatal screening program appears indispensable.

ACKNOWLEDGMENTS:

We really appreciate Professor Fatima Banu Anlar (Professor, pediatrics and pediatric neurology, Hacettepe University Faculty of Medicine, Turkey) who was a great help in writing this article and also Bandar Abbas Health center for its support in aggregation of samples and results.

CONFLICT OF INTEREST:

The authors declare that they have no conflict of interests.

FOUNDING:

The authors received financial support from Research Deputy of Hormozgan University of Medical Sciences.

AUTHORS' CONTRIBUTIONS:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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