

Epidemiological assessment of Congenital Hypothyroidism in Ilam province between 2005 -2011

Asrin Karimi^{1, 2}, Reza Beiranvand^{1, 2}, Ali Delpisheh^{1, 3*}, Kourosh Sayehmiri³, Asadollah Ehsanzadeh⁴

1. Department of Epidemiology, Faculty of Health, Ilam University of Medical Sciences, Ilam, Iran
2. Student's Research Committee, Ilam University of Medical Sciences, Ilam, Iran
3. Research Center for Prevention of Psychosocial Injuries, Ilam University of Medical Sciences, Ilam, Iran
4. Deputy of Health, Unit of Prevention of Non-Communicable Diseases, Ilam University of Medical Sciences, Ilam, Iran

*Corresponding author: Tel: +98 9183774837; fax: +98 8433342887

Address: Department of Epidemiology, Ilam University of Medical Sciences, Banganjab Avenue, Ilam, Iran

E-mail: Alidelpisheh@yahoo.com

Received 14/04/2014; revised 08/07/2014; accepted 31/08/2014

Abstract

Introduction: Congenital hypothyroidism is the most common cause of mental retardation in the world. The presence of hypothyroidism in fetal is lead to abnormalities in major organs, including nervous system and central skeleton. Aim of this study was to investigate epidemiologic situation of neonatal hypothyroidism in Ilam province between 2005 -2011.

Materials and methods: This was a cross-sectional retrospective study. The number of 27258 infants was born in Ilam province from 2005 till 2011. Among these infants who were entered to screening program of congenital hypothyroidism, about 162 cases were identified as congenital hypothyroidism patients. The data were analyzed through SPSS software.

Results: From identified patients, 95 infants (58.9%) were male. Incidence rate was 5 in 1000 live birth. There was a significant correlation between birth weight and T4 level ($P = 0.02$). The analysis showed that there is a significant relationship between gender of neonate and TSH level ($P = 0.009$).

Conclusion: Prevalence of congenital hypothyroidism in Ilam province compare to other parts of country was high. Due to the importance of hypothyroidism in mental retardation, encouraging of parents to attend screening test seems to be necessary.

Keywords: Congenital hypothyroidism, epidemiology, mental retardation

Introduction

Congenital hypothyroidism is one of the most common endocrine diseases and is the most important cause of mental retardation (1). Thyroid function is necessary for physical and mental growth of newborn(2). The Majority of newborns with hypothyroidism have normal appearance and don't have specific symptoms of disease, so if diagnose will be only according to clinical symptoms, neonates will be infected with irreversible complications such as deafness and mental retardation(3). IQ impairments caused by the disease can be prevented, when the

disease is diagnosed in the neonatal period (4, 5).

The thyroid is a small gland located in the front of the neck that produces and secretes a hormone called thyroxin that plays an important role in different cells metabolism and growth of the body. Influences of hormone are necessary for brain growth and its development. Evaluation of thyroid function is very important and in the last three decades took too much attention. Nowadays, in most countries for on time diagnosis and treatment, hypothyroid screening test is

done at the time of neonate birth (6, 7, and 8). For the First time hypothyroid screening studies started in North America (9). The first time in Iran CH screening was done by Dr. Azizi et al in 2008 (10).

Hypothyroidism screening is one of the preventive programs that benefit- cost ratio is positive. It is estimated that the cost for screening of any newborn would be 0.7 to 1.60 \$. The cost of diagnosis of a hypothyroidism neonate is 5000\$. Benefit – cost ratio in several developed countries is different from 7.11 to 1 (11).

In Iran, mentioned ratio was 15.1 (12). Prevalence of hypothyroidism in Iran is different for example: in Tehran, Shiraz, Esfahan was 1 in 914, 1 in 1433, and 1 in 370 births, respectively (13). Totally prevalence of this disease in Iran is estimated 1 in 1000 live birth. Prevalence in the world is 1 in 3000 live birth. Incidence rate of congenital hypothyroidism in Iran comparison to other countries is high (14). According to conducted studies in different parts of the world, the reasons of different prevalence of CH is due to various criteria for definite CH diagnosis, The hypothyroidism result from iodine deficiency lead to transient CH (36, 37).

Considering the fact that in most provinces, studies have been conducted about congenital hypothyroidism, but such those studies were not conducted in Ilam despite of importance of this disease.

This study was conducted to evaluate of the epidemiologic situation of congenital hypothyroidism from 2005 to 2011 in Ilam province.

Materials and methods

This study was descriptive and analytical. In this study information of patients were gathered from their documents in the Portal System of Prevention and Health Care Department of non-communicable diseases of Ilam University of Medical Sciences. By using check list, demographic variables including gender, settlement (urban or rural), birth weight,

birth height, city residence and year of birth and clinical variables, including type of delivery, previous parental illness, existence of disease in family, anomaly, TSH, T4, age of neonate in treatment starting, dose of taken drug and trend of disease, were collected

Diagnosis criteria of hypothyroidism are measurement of TSH and T4 levels. If TSH will be less than 5 mu/l test of congenital hypothyroidism is negative. If TSH level will be 5.1 – 9.9 µg/dl neonates is Suspicious to hypothyroidism, and TSH will be more than 9 mu/l is hypothyroidism. Normal range of T4 in blood is 5.6-13.7 mcg/dl, T4 level of less than 5.6 µg/dl and T4 level of more than 13.7 µg /dl is hypothyroidism (15).

If 3 years after treatment serum levels of TSH and T4 remain in the normal range is called Transient hypothyroidism. After this time any stable hypothyroidism in children with congenital hypothyroidism is permanent hypothyroidism (16).

Data were analyzed using SPSS ver.16 software. For descriptive purposes, frequency, mean and standard deviation were used. To calculate cumulative incidence, population of beginning 2005 was used. Chi-square test, independent t-test and Mann-Whitney with a significance level of less than 5% were considered to indicate a statistical significant difference.

Because population changes are negligible during two consecutive years, and the probability of every born baby being diagnosed with hypothyroidism in the community is low (p is low), and high population (n is large), Thus new cases is $n=Np$, based on Poisson distribution mean and variance is equal to n (38).

For comparison of incidence rate of congenital hypothyroidism in two consecutive years Poisson distributions can be used. N_1 is new hypothyroidism cases in second year, and n_2 is new hypothyroidism cases in first year. For incidence rate comparing of hypothyroidism during two consecutive

years in Ilam province was used above method (38).

Results

Totally among 27258 births in Ilam province from 7 cities during 2005-2011, 162 neonates diagnosed with congenital

hypothyroidism. Among these numbers more than half of those 95 neonates (58.9%) were male and fewer 65 (41.1%) were female.

Abbdanan city had the highest rate of hypothyroidism and Sirvan-Chardavel had the lowest rate of disease (Table 1).

Table 1. Incidence rate of congenital hypothyroidism in cities of Ilam province between 2005- 2011.

Name of city	Number of screened infants	Number of diagnosed CH	Incidence rate in 1000 live births
Ilam	11989	85	7
Abdanan	2470	34	13
Sirvan Chardavel	3798	8	1
Ayvan	2619	11	4
Malekshahi	1214	5	4
Mehran	1512	8	5
Dehloran	3656	11	3
Total	27258	162	5

In all cities Males were more affected to CH. Rang of TSH level of neonates was between 0.8 and 100 $\mu\text{g}/\text{dl}$. TSH mean of male (n=95) was 24.3 ± 20.6 . TSH mean of female (n=53) was 19.3 ± 23.1 . T4 mean in male was 48.2 ± 25.5 and in female was 53.4 ± 27.8 . Birth weight mean in male was $3.343\pm 0.590\text{kg}$ and in female was $3.295\pm 0.575\text{kg}$. Birth height mean in male was 48.2 ± 2.45 cm and in female was $48.8\pm 2.31\text{cm}$.

Among hypothyroidism cases TSH of 5.1% was less than $5\mu\text{g}/\text{l}$, TSH of 26.6% was 5.1-9.9 $\mu\text{g}/\text{l}$ and 68.3% was more than 9.9 $\mu\text{g}/\text{l}$. T4 of 2.5% neonates was less than $5.6\mu\text{g}/\text{dl}$, T4 of 16.1% was 5.6-13.7 $\mu\text{g}/\text{dl}$ and 81.4% had T4 level of more than 13.7 $\mu\text{g}/\text{dl}$. Relationship between TSH and gender was statistical significance by Mann-Whitney test (P=0.009). This result showed that the mean of TSH in male ($24.30\pm 20.68\mu\text{g}/\text{dl}$) was significantly more than the mean of TSH in female ($20.68\pm 19.33\mu\text{g}/\text{dl}$). There was a

significance versus correlation between TSH and T4 ($r=-0.324$, $P=0.0001$). In a way that increasing TSH cause T4 factor to reduce significantly and in some cases that TSH was very low, T4 was very high and contrary. Between birth weight and T4 level was found a significance positive correlation ($r=0.212$, $P=0.023$). The results showed a significance relationship between height and weight and TSH level ($P=0.0001$).

Among parents of patients 36 cases (22.2%) had relative degree 3, 15 cases (9.3%) had relative degree 4, and also more than half cases had no relative.

Trend of disease in 108 cases (66.6%), was transient. In 5 cases (3.1%) was permanent hypothyroidism, in 22 cases (13.6%) was treating and there was 1 case lead to death. By Poisson distribution changes in hypothyroidism rate was significance between 2010-2011 ($p<0.05$), while there was no significant difference between other years. Congenital hypothyroidism

rate was 5 in 1000 live births in Ilam province.

For 141 patients (92.2%) treatment was started in less than 28 days, for 12 patients (7.8%) treatment was started in more than 28 days.

Discussion

The Aim of this study was determination of epidemiologic aspects of congenital hypothyroidism in Ilam province between 2005 -2011. As mentioned, a study like this study hasn't been done throughout Ilam province, therefore, the data and results of this study seems to be candidate as a comprehensive report for other researches. Incidence rate of congenital hypothyroidism was 50 in 1000 live births, showing that prevalence of disease in Ilam province is high. In a study done by Hashemipour and other in Esfahan in 2004, prevalence of hypothyroidism was 1 in 370 neonates (17). In a study conducted by Ordukhani et al, in Tehran during 1997-2001, prevalence of hypothyroidism was 1 in 914 live births (18).

Also in a study conducted by Karamizadeh and Amir Hakimi in Shiraz, prevalence of congenital hypothyroidism was 1 in 1433 live births (19).

Prevalence of Hypothyroidism in different parts of the world is different, it is 1 in 67 in Nigeria (20), 1 in 781 in Pakistan (21), 1 in 918 in some of Asian families(11) and 1 in 10000 in Negro in America(23).

Compare to different prevalence of CH in Iran and other countries, prevalence in Ilam is high (5 in 1000). High incidence rate of CH compare to other parts of Iran is due to that screening of hypothyroidism in Ilam province started in 2005 and maybe it was not very precise in early years and cases in primary years were false positive, thus to clear incidence rate of CH in later years, conducting further researches is suggested .

In current study the majority of patients had no relatives. Also in a study conducted by Hashemi pour in Esfahan hypothyroidism appearance in family

marriage was not more (17). In a study conducted by Alizadeh and Colleagues in Khoy in 2009, hypothyroidism was more in neonates with family marriage (24).

Scientific resources have mentioned sex ratio about 2.1 for congenital hypothyroidism (26), but in this study sex ratio was 0.7. In a study conducted by Namakin in Khorasan in 2009, sex ratio patients' male was 0.6% more than females (31). In a study in Yazd hypothyroidism prevalence was high in males (32). In Akhvirads study in Tehran sex ratio was 1 (28). In a study done by Honarpisheh et al, sex ratio was 3.2 (29). In a study conducted in Italy relative risk female to male was 1.9 (30). In Australia this proportion was reported 2.5 to 1 (30). The majority of CH patients in our study and in a study conducted in Kurdistan (39) were male. Female gender is one of CH risk factor in references (40), but the reason of this difference in sex ratio is unclear .

The average age of infants in time of treatment starting was 16 days. Only in 1.2% treatment started more than 45 days. Start of treatment 14 days and 45 days after birth are ideal and is acceptable intervals on neonatal thyroid screening program (27-35). In a study conducted by Ozra Akhi et al in Mazandaran in 2009, the average of treatment starting was 25 days and for 11% of cases it started in more than 41 days (33).

In current study was founded a significance relationship between gender and TSH but in research of Eftekhari in Kerman there was no significance relationship (1).

Finally because of high prevalence of hypothyroidism in Ilam province and irreparable complications of disorder, encourage of parents to participate in hypothyroidism screening program and to continue treatment is necessary.

Limitation of the study: This study was retrospective and data were carried out from existing health records, therefore

missing data were due to incomplete document of patients.

Conclusion

Due to the importance of hypothyroidism in mental retardation, encouraging of

parents to attend screening test is necessary. It is recommended to conduct future studies to gain the exact incidence rate of CH in Ilam province and to find cause of higher percentage of male with CH than female in this province.

References

1. Eftekhari N, Asadikaram Gh, Khaksari M, Salari Z, Ebrahimzadeh M. [The prevalence rate of congenital hypothyroidism in Kerman/Iran in 2005 -2007]. *Kerman J Uni Med Sci*. 2008; 15(3): 243-50. (Persian)
2. Kalantari S. [Neonatal screening for congenital hypothyroidism (CH) in Rasht]. *J Guilan Uni Med Sci*. 2004; 13(50): 76-80. (Persian)
3. Gillam MP, Kopp P. Genetic regulation of thyroid development. *Curr Opin Pediatric*. 2001; 13(4): 358-63.
4. Delange F. Neonatal screening for hypothyroidism: Results and Perspectives. *Horm Res*. 1997; 48(2): 56-61.
5. Ordukhaneh A, Najafi R, Mehrab Y, Goldeste A, Padyab M, Mirmiran P, et al. [Neonatal screening for congenital hypothyroidism late but promising beginning. *Iran J Endocr Metab*]. 2003; 5(18): 133-8. (Persian)
6. Dreimane D, Varma SK. Common childhood thyroid disorders. *Indian J Pediatr*. 1997; 64: 3-10.
7. Tylek-Lemanska D, Ratajczak R, Szczepaniak B, Dziatkowiak H, Rybakowa M. [Mass screening program for congenital hypothyroidism in south-eastern Poland]. *J Pediatr Endocr Metab*. 1999; 12: 653-7. (Persian)
8. Mahachoklert WP, Phuapradit W, Siripoonya P, Charoenpol O, Thuvasethakul P, Rajatanavir R. Five-year thyrotrophic screening for congenital hypothyroidism in Ramathibodi Hospital. *J Med Assoc Thai*. 1999; 82 (1): 27-32.
9. Klett M. Epidemiology of congenital hypothyroidism. *Exp Clin Endocrinol Diabetes*. 1997;105 Suppl 4:19-23.
10. Azizi F, Oladi B, Nafarabadi M, Hajipour R. [Screening for congenital hypothyroidism diagnosis in Tehran: Effect of iodine deficiency in TSH transitory increase in newborns]. *Shahid Beheshti J Uni Med Sci* 1994; 18(1): 24-38. (Persian)
11. Shamshiri AR, Yarahmadi S, Forouzanfar MH, Haghdoost AA, Hamzehloo G, Holakouie Naieni K. Evaluation of current guthrie TSH cut-off point in Iran congenital hypothyroidism screening program: a cost-effectiveness analysis. *Arch Iran Med*. 2012;15(3):136-41.
12. Delavari AR, Yarahmadi S, Birjandi R, Mahdavi AR, Norouzi Nejad A, Dini M. Cost- Benefit analysis of the neonatal screening program implementation for congenital hypothyroidism in Iran. *Int J Endocr Metab*. 2006; 4(1): 84-7.
13. Azizi F. [Screening for congenital hypothyroidism: late but promising]. *J Endocr Metab*. 2004; 6(1): 1-3. (Persian)
14. Kligman RM, Stanton BF, ST. Geme JW, Schor NF, Behrman RE. *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia: Elsevier, Saunders; 2011. P. 1895-6.
15. Davari A, Yarahmadi Sh, Mahdavi hazaveh A, Nowruzi nezhad A, et al. *Hypothyroidism Disease*. Tehran: Department of Treatment and Medical

- Training, Diseases Controlling Center;2007. P.2-3.
16. Clague A, Thomas A. Neonatal biochemical screening for disease. *Clin Chim Acta*. 2002; 315: 99-110.
 17. Hashemipour M, Amini M, Iranpour R, Javadi A, Sadri Qh, et al. [High prevalence of congenital hypothyroidism in Isfahan]. *Iran J Endocr Metab* 2004; 6(1): 13-9. (Persian)
 18. Ordukhani A, Mirmiran P, Hedayati M, Hajipour R, Azizi F. [Reports of Descriptive and Etiologic Results 1997-2001]. *Iran J Endocr Metab*. 2004; 4(3): 153-160. (Persian)
 19. Karamizadeh Z, Amirhakimi GH. [Incidence of Congenital Hypothyroidism in Fars province, Iran]. *Iran J Med Sci*. 1992; 17(3): 78-80. (Persian)
 20. Ojule AC, Osotimehin OB. Maternal and neonatal thyroid status in Saki, Nigeria. *Afr J Med Sci*. 1998; 27: 57-61.
 21. Hall SK, Hutchesson AC, Krik JM. Congenital hypothyroidism, seasonality and Consanguinity in the West Midlands, England. *Acta Prediatr*. 1999; 88(4): 212-5.
 22. Rosenthal M, Addison GM, Price DA. Congenital hypothyroidism: increased incidence in Asian families. *Arch Dis Child*. 1988; 63(7): 790-3.
 23. Robert HE, Moore CA, Fernhoff PM, Brown AL, Khouri MJ. Population Study of Congenital Hypothyroidism and Associated Birth Defects, Atlanta, 1979-1992. *Am J Med Genet*. 1997; 71(8): 29-32.
 24. Safaralizadeh F, Sadifi R, Partoazam H. [Frequency of congenital hypothyroidism and relationship with some risk factors in health-treatment centers in Khoy, 2006-2007]. *Orumiye J Obstetr Nurs*. 2009; 8(1): 35-9. (Persian)
 25. Kalantari S. [Neonatal screening for congenital hypothyroidism diagnosis in Rasht]. *Guilan J Uni Med Sci*. 2004; 13 (50):142-8. (Persian)
 26. Foley TP Jr. Congenital hypothyroidism. In: Braver man LE, Utiger RD, editors. *Warner and Ingbars the Thyroid: A fundamental and clinical text*. 8th ed. Philadelphia: Lippincott Williams and Wilkins; 2000. P. 977-83.
 27. Delange F. Screening for congenital hypothyroidism used as an indicator of the degree of iodine deficiency and of its control. *Thyroid*. 1998; 8(12): 1185-92.
 28. La Franchi St. Hypothyroidism In: Behrman R, Kliegman R, Jenson H, editors. *Nelson textbook of pediatrics*. 17th ed. Saunders Company; 2004.P.1872-6.
 29. Akhavirad MB, Rafati Sh, Borna H, Zaeri F, Safabakhsh M. [Assessment of neonatal hypothyroidism frequency with indirect hyperbilirubinmi]. *Med Daneshvar Sci-Res J*. 2007;5(2): 70-7. (Persian)
 30. Honarpiشه A. Frequency of congenital hypothyroidism among neonates with prolonged jaundice in Khashan. *Tebbo Tzkiye*; 2003.
 31. Namkin K, Sedighi E, Sharifzadeh G, Zardast M. [Prevalence of congenital hypothyroidism in south Khorasan province]. *J Birjand Uni Med Sci*. 2012; 19(2): 191-9. (Persian)
 32. Nourishadkam M, Jafarizadeh M, Mirzaei M. [Prevalence of Hypothyroidism and increasing TSH transitory in Yazd province]. *Sedoghi Yazd J Uni Med Sci*. 2008; 16(3): 15-20. (Persian)
 33. Akhi O, Shabani M, Kosaryan M, Qhafari V, Sajadisaroi N. [Prevalence assessment of congenital hypothyroidism in Mazandaran province (2007-2008)]. *Mzandaran J Uni Med Sci*. 2011; 21(84): 72-9. (Persian)
 34. Mengreli C, Kassiou K, Tsagaraki S, Pantelakis S. Neonatal screening for

- hypothyroidism in Greece. *Eur J Pediatr.* 1981; 137(2): 185-7.
35. Fisher DA. Disorder of the Thyroid in the newborn and infant. In: Sperling MA ed. *Pediatrics endocrinology* 1st ed. Philadelphia: W.B.Saunders Company; 1996.P.51-70.
36. Leger J, Marinovic D, Garel C, Bonaiti-Pellie C, Polak M, Czernichow P. Thyroid development anomalies in first degree relatives of children with congenital hypothyroidism. *J Clin Endocr Metab.* 2002; 87 (2): 575-80.
37. Castanet M, Polak M, Bonaiti-Pellie C, Lyonnet S, Leger J, Czernichow P. On behalf of AFDPHE (Association Française pour le dépistage et al prevention des handicaps de l'Enfant). Nineteen years of national screening for congenital hypothyroidism: familial cases with thyroid dysgenesis suggest the involvement of genetics factors. *J Clin Endocr Metab.* 2001; 86(5): 2009-14.
38. Khorshidi A, Sayehmiri K. The impact of public partnership on identifying patients with Tuberculosis in Darrehshahr, Iran. *Iran J Epi.* 2011; 6(4): 1-7.
39. Esmailnasab N, Moasses Qhafari B, Afkhamzadeh A. [Risk Factors of Congenital Hypothyroidism in neonates of Kurdistan province]. *Kurdistan J Uni Med Sci.* 2012;6(3): 103-8.
40. Medda E, Olivier A, Stazi MA, Grandolfo ME, Fazzini C, Baserga M, et al. Risk factors for congenital hypothyroidism: results of a population case- control study (1997-2003). *Eur J Endocr.* 2005; 153(5): 765-73.