Chronic Diseases Journal

DOI: 10.22122/cdj.v7i3.411

Published by Vesnu Publications

The incidence of permanent congenital hypothyroidism: A systematic review and meta-analysis

Asrin Karimi[1], Maryam Parvareh[1], Ghobad Moradi[1], Bijan Nouri[1], Parvin Allahyari[1]

1 Social Determinants of Health Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran

Review Article

Abstract

BACKGROUND: One of the most prevalent endocrine disorders is congenital hypothyroidism (CH). The most important complication of this disorder is mental retardation. This study was carried out to evaluate CH prevalence based on newborn screening of CH in different countries through a meta-analysis study.

METHODS: The researchers in this study searched the literature among PubMed/Medline, Scopus, Google Scholar, ISI Web of Sciences and Web of Knowledge, and Science Direct databases. The evaluations were carried out using a researcher-made checklist including goals and research questions. Meta-regression with the Mantel-Haenszel method was performed using a random effects model and Egger's test (ET) and Begg's test (BT) by the STATA software.

RESULTS: A total of 10875 studies were found in the initial literature search related to CH. Ultimately, based on the eligibility criteria considered in the present study, 25 studies were categorized as qualified for systematic review and meta-analysis. The estimate of the CH prevalence among the screened neonates in the studies based on the random effects model was 4.85 per 10000 [95% confidence interval (CI): 4.04- 5.66].

CONCLUSION: Due to the importance of CH related diseases especially for detection of type of hypothyroidism, it is necessary more surveillance be carried out in all countries. Based on Different studies, recognition of the most CH patients is before age 1 year so it helps to reduction the risks of developmental delay, and delayed physiological development and mental retardation.

KEYWORDS: Congenital Hypothyroidism, Hypothyroidism, Prevalence, Meta-Analysis

Date of submission: 19 July 2018, ***Date of acceptance:*** 12 Sep. 2018

Citation: Karimi A, Parvareh M, Moradi G, Nouri B, Allahyari P. **The incidence of permanent congenital hypothyroidism: A systematic review and meta-analysis.** Chron Dis J 2019; 7(3): 207-213.

Introduction

One of the most prevalent disorders in children is congenital hypothyroidism (CH). Newborn screening for CH has been addressed in developed countries for more than 40 years. However, this plan has been started in developing countries in recent years.[1] The first CH screening was conducted in North America. Screening helps early diagnosis of infants with CH and prevents side effects resulting from this complication. Since most of the infants with CH have normal appearance with no sign of disease, they can be identifed through blood test for CH.[2] It is estimated that 25% of 127 million of birth population worldwide undergo CH screening.[3] Given the preventable and treatable nature of this disorder, it is clear that delay in treatment of CH may cause neurological and intelligence quotient (IQ) problems.[4] The most usual type of CH is primary hypothyroidism which is diagnosed by T4 and thyroid-stimulating hormone (TSH) levels, so infants must be diagnosed properly and treated quickly to prevent permanent CH and physical delays.[5] It

Corresponding Author:
Asrin Karimi
Email: karimi.asrin@gmail.com

is notable that some parents of the children with CH discontinue thyroid hormone replacement based on the inappropriate medical advice and sometimes without a follow-up.[6] Incidence rates of CH vary in different parts of the world and in various times. It was reported in the range of 1:1000 to 1:4000[7]. Based on a study in French during the 20-year period, the permanent CH incidence was 1:10000, while this rate was found to be about 1:1800 in Greece over an 11-year period. There is some evidence that CH incidence has been increased from 1:4094 to 1: 2372 in the United States in 1987 and 2002, respectively. One justifying reason is changes in the diagnostic strategies.[8] There have been numerous studies carried out worldwide with different prevalence rates of CH, therefore the aim in this study was to evaluate the overall prevalence of CH through a systematic review and meta-analysis.

Materials and Methods

The study researchers searched and identified studies on CH with reports regarding the children with CH diagnosed during neonate screening program all around the world from January 1, 2010 to June 8, 2016. All the eligible studies were listed by searching the international databases such as Google Scholar, Scopus, PubMed/Medline, Web of Science, and Science Direct. Various combinational terms were searched for to find a large range of literature, including: "Congenital hypothyroidism" "Congenital hypothyroidism and prevalence", "Congenital hypothyroidism and incidence", and "Congenital hypothyroidism and epidemiology"; the search was limited to no patent and in the 2010-2016 period in the Google Scholar. Moreover, to search in PubMed, all studies in English on human with medical subject headings (MeSH), in the abstract, title, and text were investigated.

All essential data from the listed references were investigated by two of the researchers (Asrin Karimi1 and Maryam Parvareh). Appraisal was performed using a checklist containing the study objectives and other research questions. Some studies with no inclusion criteria were deleted.

The following information was extracted from the enrolled studies: year of study, number of detected newborns with permanent CH, sample size, country, author, and title based on the standardized form. The prepared data was reviewed twice by two reviewers independently. All gathered articles were assessed according to the critical checklists STROBE and MOOSE.

Data analysis was performed using the STATA software version 12. Heterogeneity of the studies was appraised by the I^2 statistics. This value was $I^2 = 98.4\%$ ($P < 0.100$). The I^2 statistic was employed to evaluate the percentage of the observed variability due to heterogeneity rather than chance and varied from 0 to 100%, with values of 0% and 100% expressing no observed heterogeneity and significant heterogeneity, respectively. The random model was used while $I^2 > 50\%$, otherwise the fixed effect model was performed. Thus, the random model was used due to $I^2 > 50\%$.[9] The presence of study bias was determined by the funnel plot and conducting the Begg's test. $P < 0.050$ was considered to indicate a statistically significant difference. Furthermore, the univariate approach was employed to evaluate the causes of heterogeneity among the studies and the Egger test was conducted to assess potential study bias.

Results

A total of 10875 studies were found in the initial literature search related to CH. After precise screening of the abstract, title, and text of some of the studies, 10782 ones did not meet the inclusion criteria and some were duplicated, hence they were excluded and

about 93 articles were selected for reading carefully. Ultimately, based on the eligibility criteria considered in the present study, 25 studies were categorized as qualified for systematic review and meta-analysis (Figure 1) (Table 1).

The estimate of the CH prevalence among the screened neonates in the studies based on the random effects model was 4.85 per 10000 [95% confidence interval (CI): 4.04- 5.66] (Figure2). According to the meta-regression graphs (Figure 3), there was no relationship between the prevalence of CH and year of publication of the studies (P = 0.440) and the prevalence of CH and sample size (P = 0.300) (Figure 4). Thus, the prevalence of CH among the screened neonates did not change based on the year of publication of the studies and the sample size significantly.

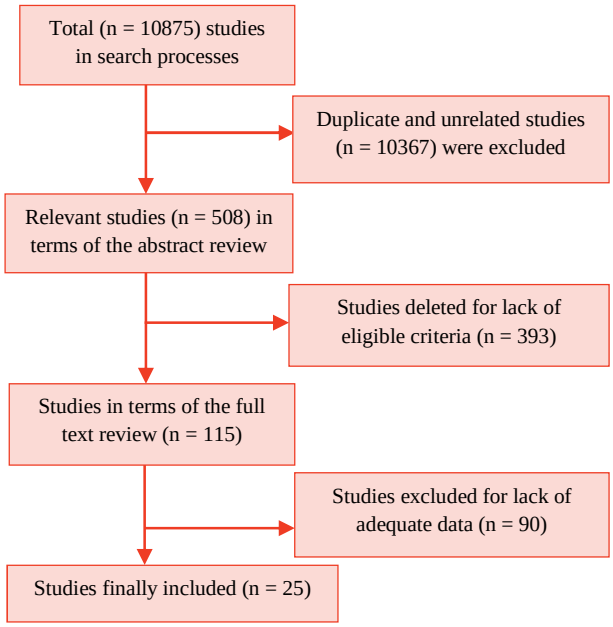

Figure 1. Flow of data in different phases of the systematic review

Table 1. Characteristics of the studies selected

Authors	Study area	Number of neonates screened	Number of neonates with permanent CH
Bekhit and Yousef[10]	Egypt	731743	204
Zhao et al.[11]	China	5142148	1922
Deladoey et al.[12]	Canada	1660857	620
Hettiarachchi and Amarasena[13]	Sri Lanka	78,167	47
Palhares et al.[14]	Brazil	32278	16
Anastasovska et al.[15]	Macedonia	9757	8
Al Hosani et al.[16]	UAE	698 629	373
Chen et al.[4]	Taiwan	3000000	1482
Ascurra et al.[17]	Paraguay	53360	35
Al-Jurayyan and Al Jurayyan[18]	Saudi Arabia	1,007,350	306
Samardzic et al.[19]	Montenegro	40758	17
Kaur et al.[20]	India	6813	5
Kocova et al.[21]	Macedonia	215077	83
Cornejo et al.[22]	Chile	2,478,123	273
Wintergerst et al.[5]	America	751,144	409
Aminzadeh et al.[23]	Iran	47,075	142
Golbahar et al.[24]	Bahrain	17806	6
Atas et al.[25]	Konya-Turkey	93,897	43
Juan-Fita et al.[26]	Spain	71,595	38
Kusdal et al.[27]	Kocaeli-Turkey	28,188	39
Hussain et al.[28]	Malaysia	12928	2
Sun et al.[29]	China	442,454	183
Gopalakrishnan et al.[30]	India	13426	11
Woo et al.[31]	America	92,800	11
Cameo et al.[32]	Colombia	34,363	19

CH: Congenital hypothyroidism; UAE: United Arab Emirates

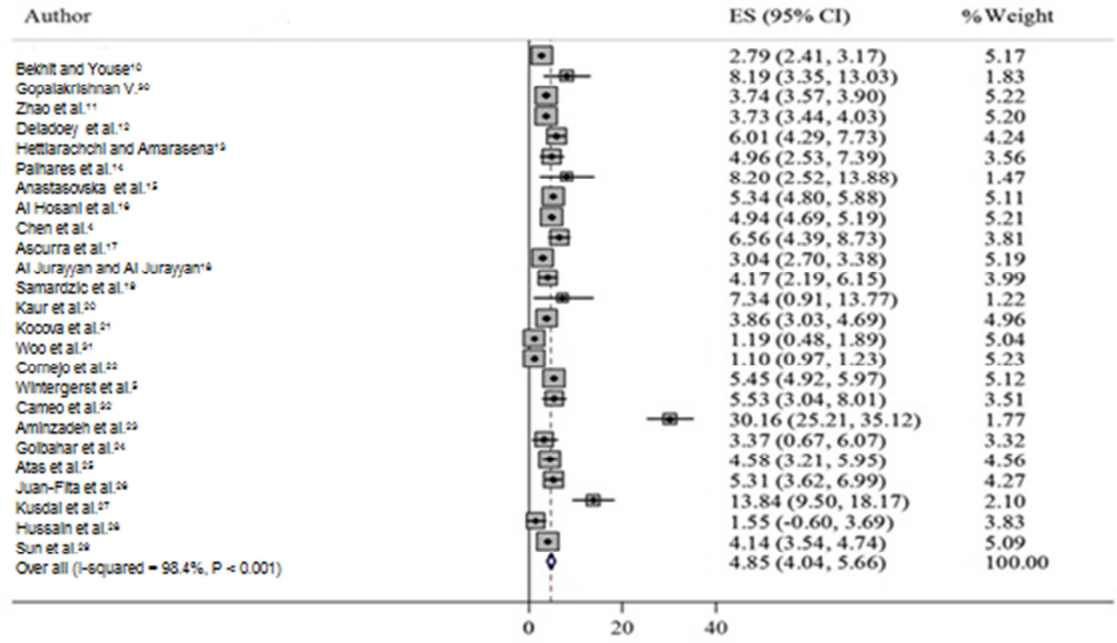

Figure 2. Forest plot of the prevalence of the studies on congenital hypothyroidism (CH) conducted worldwide in the 2010-2018 period

CI: Confidence interval

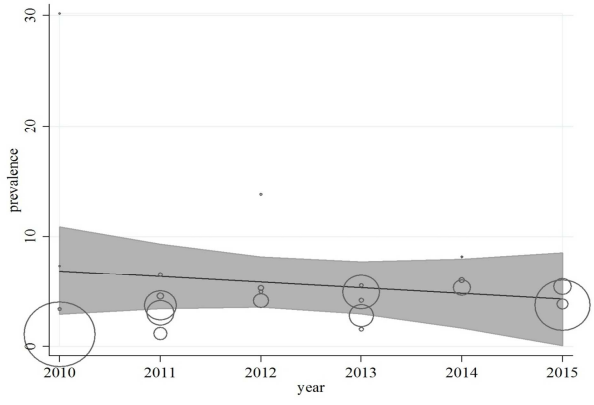

Figure 3. Meta-regression plot of congenital hypothyroidism (CH) prevalence based on the year of publication

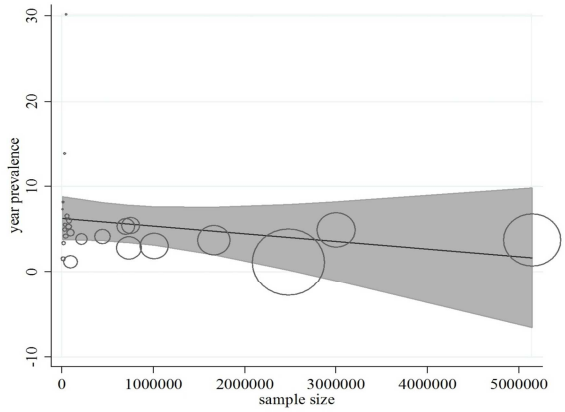

Figure 4. Meta-regression plot of congenital hypothyroidism (CH) prevalence based on the sample size

The Egger's test was performed to assess the small study effect (P < 0.001).

Discussion

The current study reported a systematic review and meta-analysis on the CH screening program in newborn children based on 25 sample studies among a total of 14793617 neonates.

As it seems, it is the first time that the prevalence of CH is reported considering all studies published in this field worldwide. The pilot CH screening was implemented in 1972 in North America for the first time.[33] In this study, the overall prevalence of the permanent CH was 4.85:10000 neonates. Meanwhile, the studies conducted in other parts of the world

have reported an incidence rate of 1-50% for the transient CH among the children with CH.[34] It is accepted that about 10-15% of the children diagnosed of the primary CH have transient type of CH at last.[35] Different fractions of the incidence of the two types of CH has been reported from different countries with different cultures, nations, and races.[6,36] In addition, the incidence of total CH varies in different parts of the world. For instance, a CH incidence rate of 1:10,000 vs. 1:2000 has been reported among the blacks in comparison with the Hispanic and native American people, respectively.[14] Transient CH may be the result of some maternal factors such as the excessive iodine intake, iodine deficiency, anti-thyroid medication, or existence of antibodies against thyroid tissue during pregnancy. One of the limitations of the study was that the different incidence rates of the permanent CH reported in different studies may be unreliable, because confirmation of the permanent CH needs to follow up patients for 3 years after the first diagnosis. The prevalence of CH is significantly depending on the study area, thus it is important that countries report correct and accurate information in other to make decisions about the deployment of the best solutions and conduct more studies to gain knowledge on the cause of CH in those areas. In some studies, the incidence of permanent CH was higher than that of the transient CH. The prevalence of permanent and transient CH was 1:3587 and 1:16667 live births, respectively.[14] Other limitations were observed in the studies found based on the search, as most of them did not distinguish children based on gender after determining the type of CH (transient or permanent). Some studies indicated thatch the CH incidence was higher in girls compared to boys.[4,37] It was found in recent studies that practically all screening programs report a predominance for the female gender, about 2:1 female-to-male ratio.[38] The female/male ratio varies in different studies, for instance, it was 19.6% higher among women than men[4] and 3:1 in Saudi Arabia.[38] A male preponderance of 1:1.41 was also reported in a study in East Azerbaijan Province, Iran, probably due to the high prevalence of consanguineous marriages.[38] Different studies have reported a variety of CH incidence trend over time, for instance in a study[10] conducted in Taiwan, the CH incidence increased by 10% from 1997 to 2004 and decreased after 2005. The peak incidence rate in the 1997-2008 period in this population was 7.68:10000 infants in 2001. The female/male ratio differed during the 12 years of study. In comparison with the present study, this study did not show significant incidence of CH over the study period. That may be due to the diagnosis criteria or registry systems.

Conclusion

More surveillance of CH-related diseases, especially for detection of the type of hypothyroidism needs to be carried out in the future. Data obtained from the studies on patients with CH show that most of the patients with CH are diagnosed before the age of 1 year and that early diagnosis can decrease the risks of developmental delay, mental retardation, and delayed physiological development.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

This work was supported by a research grant from deputy research of Kurdistan University of Medical Sciences, Sanandaj, Iran. The authors would like to appreciate their financial support. The grant number is "IR.MUK. REC.1394.355".

References

1. Abduljabbar MA, Afifi AM. Congenital hypothyroidism. J Pediatr Endocrinol Metab 2012; 25(1-2): 13-29.

2. Yang R, Gao W, Li R, Zhao Z. Effect of atomoxetine on the cognitive functions in treatment of attention deficit hyperactivity disorder in children with congenital hypothyroidism: A Pilot Study. Int J Neuropsychopharmacol 2015; 18(8).
3. Rastogi MV, LaFranchi SH. Congenital hypothyroidism. Orphanet J Rare Dis 2010; 5: 17.
4. Chen CY, Lee KT, Lee CT, Lai WT, Huang YB. Epidemiology and clinical characteristics of congenital hypothyroidism in an Asian population: A nationwide population-based study. J Epidemiol 2013; 23(2): 85-94.
5. Wintergerst K, Gembel G, Kreipe T, Zeller P, Eugster E, Young B, et al. Congenital hypothyroidism long-term follow-up project: Navigating the rough waters of a multi-center, multi-state public health project. J Genet Couns 2015; 24(3): 464-72.
6. Korzeniewski SJ, Grigorescu V, Kleyn M, Young WI, Birbeck G, Todem D, et al. Transient hypothyroidism at 3-year follow-up among cases of congenital hypothyroidism detected by newborn screening. J Pediatr 2013; 162(1): 177-82.
7. Fisher DA. Second international conference on neonatal thyroid screening: Progress report. J Pediatr 1983; 102(5): 653-4.
8. Dilli D, Czbas S, Acican D, Yamak N, Ertek M, Dilmen U. Establishment and development of a national newborn screening programme for congenital hypothyroidism in Turkey. J Clin Res Pediatr Endocrinol 2013; 5(2): 73-9.
9. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002; 21(11): 1539-58.
10. Bekhit OE, Yousef RM. Permanent and transient congenital hypothyroidism in Fayoum, Egypt: A descriptive retrospective study. PLoS One 2013; 8(6): e68048.
11. Zhao DH, Shen Y, Gong JM, Meng Y, Su L, Zhang X. Newborn screening for congenital hypothyroidism in Henan province, China. Clin Chim Acta 2016; 452: 58-60.
12. Deladoey J, Ruel J, Giguere Y, Van Vliet G. Is the incidence of congenital hypothyroidism really increasing? A 20-year retrospective population-based study in Quebec. J Clin Endocrinol Metab 2011; 96(8): 2422-9.
13. Hettiarachchi M, Amarasena S. Indicators of newborn screening for congenital hypothyroidism in Sri Lanka: Program challenges and way forward. BMC Health Serv Res 2014; 14: 385.
14. Palhares HM, Silva LC, Sato LM, Lara BH, Miranzi SS, Silva Ade P, et al. Incidence of congenital hypothyroidism in the city of Uberaba/Minas Gerais and etiological evaluation of the affected subjects. Arq Bras Endocrinol Metabol 2012; 56(5): 305-12.
15. Anastasovska V, Koviloska R, Kocova M. High incidence of congenital hypothyroidism in one region of the republic of macedonia. Balkan J Med Genet 2014; 17(1): 31-6.
16. Al Hosani H, Salah M, Osman HM, Farag HM, El-Assiouty L, Saade D, et al. Expanding the comprehensive national neonatal screening programme in the United Arab Emirates from 1995 to 2011. East Mediterr Health J 2014; 20(1): 17-23.
17. Ascurra M, Rodriguez S, Valenzuela A, Blanco F. Incidencia de hipotiroidismo congenito en 14 regiones sanitarias del Paraguay. Rev Chil Pediatr 2011; 82(4): 360-1. [In Spanish].
18. Al Jurayyan NA, Al Jurayyan RN. Congenital hypothyroidism and neonatal screening in Saudi Arabia. Curr Pediatr Res 2011; 16(1): 31-6.
19. Samardzic M, Gligorovic-Barhanovic N, Popovic N, Popovic-Samardzic M. Newborn screening program for congenital hypothyroidism in Montenegro. Paediatrics Today 2013; 9(2): 158-62.
20. Kaur G, Srivastav J, Jain S, Chawla D, Chavan BS, Atwal R, et al. Preliminary report on neonatal screening for congenital hypothyroidism, congenital adrenal hyperplasia and glucose-6-phosphate dehydrogenase deficiency: A Chandigarh experience. Indian J Pediatr 2010; 77(9): 969-73.
21. Kocova M, Anastasovska V, Sukarova-Angelovska E, Tanaskoska M, Taseva E. Clinical practice: experience with newborn screening for congenital hypothyroidism in the Republic of Macedonia - a multiethnic country. Eur J Pediatr 2015; 174(4): 443-8.
22. Cornejo V, Raimann E, Cabello JF, Valiente A, Becerra C, Opazo M, et al. Past, present and future of newborn screening in Chile. J Inherit Metab Dis 2010; 33(Suppl 3): S301-S306.
23. Aminzadeh M, Chomeili B, Riahi K, Dehdashtian M, Cheraghian B, Valavi E. Effect of temperature changes on the occurrence of congenital hypothyroidism. J Med Screen 2010; 17(3): 121-4.
24. Golbahar J, Al-Khayyat H, Hassan B, Agab W, Hassan E, Darwish A. Neonatal screening for congenital hypothyroidism: A retrospective hospital based study from Bahrain. J Pediatr Endocrinol Metab 2010; 23(1-2): 39-44.
25. Atas B, Altunhan H, Ata E, Musevitoglu A. Frequency of congenital hypothyroidism in neonates in the Konya region, Turkey. J Pediatr Endocrinol Metab 2011; 24(3-4): 139-40.
26. Juan-Fita MJ, Egea-Mellado JM, Gonzalez-Gallego I, Moya-Quiles MR, Fernandez-Sanchez A. Expanded newborn screening in the Region of Murcia, Spain. Three-years experience. Med Clin (Barc) 2012;

139(13): 566-71.
27. Kusdal Y, Yesiltepe-Mutlu G, Ozsu E, Cizmecioglu FM, Hatun S. Congenital hypothyroidism screening program in Turkey: A local evaluation. Turk J Pediatr 2012; 54(6): 590-5.
28. Hussain S, Taib MNA, Zainol AR. Audit of Newborn Screening Programme for Congenital Hypothyroidism. International Medical Journal 2013; 20(5): 633-4.
29. Sun Q, Chen YL, Yu ZB, Han SP, Dong XY, Qiu YF, et al. Long-term consequences of the early treatment of children with congenital hypothyroidism detected by neonatal screening in Nanjing, China: A 12-year follow-up study. J Trop Pediatr 2012; 58(1): 79-80.
30. Gopalakrishnan V, Joshi K, Phadke S, Dabadghao P, Agarwal M, Das V, et al. Newborn screening for congenital hypothyroidism, galactosemia and biotinidase deficiency in Uttar Pradesh, India. Indian Pediatr 2014; 51(9): 701-5.
31. Woo HC, Lizarda A, Tucker R, Mitchell ML, Vohr B, Oh W, et al. Congenital hypothyroidism with a delayed thyroid-stimulating hormone elevation in very premature infants: Incidence and growth and developmental outcomes. J Pediatr 2011; 158(4): 538-42.
32. Cameo T, Gumer LB, Williams KM, Gomez J, McMahon DJ, Oberfield SE. A retrospective review of newborn screening for congenital hypothyroidism and newborn thyroid disease at a major medical center. Clin Pediatr (Phila) 2013; 52(11): 1054-8.
33. Fisher DA, Dussault JH, Foley TP Jr, Klein AH, LaFranchi S, Larsen PR, et al. Screening for congenital hypothyroidism: Results of screening one million North American infants. J Pediatr 1979; 94(5): 700-5.
34. Weber G, Vigone MC, Passoni A, Odoni M, Paesano PL, Dosio F, et al. Congenital hypothyroidism with gland in situ: Diagnostic re-evaluation. J Endocrinol Invest 2005; 28(6): 516-22.
35. Connelly JF, Coakley JC, Gold H, Francis I, Mathur KS, Rickards AL, et al. Newborn screening for congenital hypothyroidism, Victoria, Australia, 1977-1997. Part 1: The screening programme, demography, baseline perinatal data and diagnostic classification. J Pediatr Endocrinol Metab 2001; 14(9): 1597-610.
36. Ordookhani A, Mirmiran P, Moharamzadeh M, Hedayati M, Azizi F. A high prevalence of consanguineous and severe congenital hypothyroidism in an Iranian population. J Pediatr Endocrinol Metab 2004; 17(9): 1201-9.
37. Al-Maghamsi MS, Al-Hawsawi ZM, Ghulam GN, Okasha AM. Screening for congenital hypothyroidism in North-West region of Saudi Arabia. Saudi Med J 2002; 23(12): 1518-21.
38. Zeinalzadeh AH, Talebi M. Neonatal screening for congenital hypothyroidism in East Azerbaijan, Iran: The first report. J Med Screen 2012; 19(3): 123-6.