Asian Journal of Medicine and Health
3(3): 1-8, 2017; Article no.AJMAH.31934

SCIENCEDOMAIN *international*
www.sciencedomain.org

Prevalence of Transient Congenital Hypothyroidism as Seen at the University of Port Harcourt Teaching Hospital, Nigeria

O. Otokunefor[1*], C. G. Orluwene[1] and V. C. Wakwe[1]

[1]Department of Chemical Pathology, University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Author OO designed the study, performed the statistical analysis, wrote the protocol, wrote the first draft of the manuscript and did the sample collection. Authors CGO and VCW managed the proof reading of the manuscript. Author VCW contributed to the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJMAH/2017/31934
Editor(s):
(1) Janvier Gasana, Department of Environmental & Occupational Health, EO Epidemiology, and EO Medicine, Robert Stempel College of Public Health & Social Work, Florida International University, USA.
Reviewers:
(1) Araceli Loste, University of Zaragoza, Spain.
(2) Babatunde Kayode-Adedeji, Royal Hospital for Children, Glasgow, UK.
(3) Alphonsus N. Onyiriuka, University of Benin, Nigeria.
(4) Belisario Dominguez-Mancera, University Veracruz, Mexico.
Complete Peer review History: http://www.sciencedomain.org/review-history/18295

Short Research Article

Received 31st January 2017
Accepted 14th March 2017
Published 22nd March 2017

ABSTRACT

Aim: This study determined the prevalence of transient congenital hypothyroidism at the University of Port Harcourt Teaching Hospital. (UPTH)
Congenital hypothyroidism is one of the commonest causes of preventable mental retardation. About 85% of cases of congenital hypothyroidism are sporadic. Most of the affected neonates show no clinical features at birth. Screening programs have been established in many developed countries but data in Nigeria is sparse.
Study Design: A descriptive cross sectional study was conducted on 436 neonates between January and December, 2014.
Place and Duration of the Study: This took place between January and December, 2014 in the University of Port Harcourt Teaching Hospital.
Methods: Serum from cord blood samples was assayed for thyroid stimulating hormone (TSH) and

**Corresponding author: E-mail: mayslady@hotmail.com;*

those with increased levels had follow up assay for free thyroxine (free T_4).
Results: A total of 436 neonates were screened. Twenty-seven of them had increased TSH levels and six of those with increased TSH levels had low free T_4 concentrations. The risk factors identified by history taking did not show a statistically significant association.
Conclusion: The prevalence of transient primary congenital hypothyroidism was 1.4%. This is higher than that found in most parts of the world and similar to studies done previously in Nigeria.

Keywords: Congenital hypothyroidism; neonates; prevalence; risk factors; teaching hospital Nigeria.

1. INTRODUCTION

Congenital hypothyroidism (CH) is defined as insufficient thyroid hormone levels in newborn babies. It is relatively common in many parts of the world with a prevalence as low as 1 in 3000 in the United States [1] and as high as 1 in 420 [2] in Iran.

It is also recognised as one of the most common preventable causes of mental retardation [3,4].

The defect is usually permanent and early detection with adequate treatment prevents disability. Childhood thyroid disorders in Nigeria have not been sufficiently investigated [5,6]. Undiagnosed CH has grave consequences. This includes irreversible neurological problems, severe impairment of linear growth and permanent mental retardation [7,8,9]. People with severe mental retardation, tend to be dependent and constitute a heavy social and financial burden on their family members and the society.

Studies done previously in Nigeria found that the incidence of neonatal chemical hypothyroidism was 1.5% in Saki, a town in western Nigeria,[10] 16.8% in Bassa, (a town in Northern Nigeria with endemic goitre) and 3.8% in Jos (a town in the middle belt region of Nigeria) [11].

A comparative study done in Europe, Canada and Australia established that as many as 30% of patients with delayed diagnosis would need to be institutionalised, 20% would have profound mental retardation, while a staggering 65% would have an intellectual capacity at or below the lower borderline [12]. It is far cheaper and easier to detect and treat congenital hypothyroidism early than to manage the complications later in life [3,13]. A biochemical diagnosis of congenital hypothyroidism is made when the value of TSH is greater than 10 mIU/L and the free T_4 is lower than 0.8 ng/dl at one month of age.

The present study assessed the prevalence of CH in the University of Port Harcourt Teaching Hospital (UPTH) Rivers State, as to the best of our knowledge, no such screening program has been carried out in this part of the country.

1.2 Objectives

1. To determine the prevalence of CH among newborn babies delivered at UPTH within the study period.
2. To measure the serum TSH and Free T_4 in mothers of hypothyroid newborn babies delivered in UPTH within the study period.
3. To describe the anthropometric features and identify risk factors of newborn babies delivered in UPTH with CH in the study period.

2. MATERIALS AND METHODS

2.1 Study Organization and Participants

The study was a descriptive cross sectional epidemiological study conducted at the University of Port Harcourt teaching hospital, Rivers State, which is an academic tertiary hospital in the South-South zone of Nigeria. River State is a southern state in Nigeria. It houses the major oil drilling regions in the country. The teaching hospital is a tertiary hospital though it offers primary, secondary and tertiary services.

The department of Obstetrics and Gyneacology records an annual birth rate of about 2500 live births when there is uninterrupted health care delivery [14,15]. The chemical pathology laboratory receives 90-120 samples per day and it is well equipped. In addition to the basic equipment it also has two ELISA plate multi readers, two chemistry analysers and two Ion selective electrodes.

The sample size was calculated using the Cochran formula and the number obtained was 230. All live births in the hospital were targeted. Four hundred and thirty six specimen were

obtained over a period of one year (2014) using purposive sampling method Healthy newborns whose mothers gave informed consent were included. The following categories of newborns were excluded; those born to mothers who had any form of thyroid disorder or a family history of a thyroid disorder or who were on medication that could interfere with thyroid function as well as newborns who were sick, who had respiratory or cardiopulmonary disorders and birth asphyxia.

Cord blood specimen was obtained immediately after birth. The placenta was delivered, the clamp was removed and 5 mls of blood was allowed to flow out into a plain specimen bottle.

Three millilitres of venous blood was obtained from the mothers. The specimen was allowed to stand for 3 hours, centrifuged, separated and frozen at -20 degrees. Analysis was done in batches every 2 weeks.

Thyroid stimulating hormone (TSH) and free Thyroxine fT_4 were assayed using sandwich and competitive Enzyme Linked Immunosorbent Assay methods respectively. (Accu-Bind ELISA Microwells and Pishtaz Teb Diagnostics) A two step approach of making a diagnosis of congenital hypothyroidism was used. This involved an initial screening step using in our case cord blood and a confirmatory step which made use of venous blood. An initial TSH screen was used because TSH estimation is more sensitive for thyroid disorders [16], has a lower rate of false positives [24], and is less affected by perinatal factors [17].

Those samples found to have increased TSH levels were assessed for free T_4. Newborns with increased TSH and reduced free T_4 were recalled for confirmation. They returned before one month of age. It has been found that there is no statistical difference between the value of TSH assessed in cord blood at birth, serum TSH at birth and serum TSH assessed on the third day of life [18].

The cut off for TSH is usually specific to a country or region and is chosen sometimes using percentiles and at other times due to the researchers experience to minimize the false positive recall rates. The worldwide cut off ranges from 10 to 40 mIU/L. In Pakistan and Iran it is 20.0 mIU/L [19], 25.1 mIU/L in South Africa [20] and 15 mIU/L in Hong Kong, India and Turkey [21].

A neonate is said to have a positive screen when the TSH value is above 15 mIU/L and a diagnosis of Congenital hypothyroidism is made when there is a repeat TSH value of greater than 10 mIU/L [17] and a free T_4 of less than 8ng/dl at 4 weeks [22].

Most screening programs use blood spots from heel pricks on filter paper to screen between days 3 to 5 of life. This study made use of cord blood obtained at birth. Cord blood is easy to collect, the sample is readily available and collection is non-invasive. Collection of samples at birth is practical and suitable for our environment (as in some other African countries) [23] where prolonged hospital stay is discouraged as women with uneventful spontaneous vaginal deliveries are discharged within 24 hours. Obtaining samples at birth precedes the post natal TSH surge [24].

Data was collected using an interviewer administered questionnaire. Information obtained from the questionnaire was entered into an excel sheet. Statistical analysis was done using SPSS version 17. Continuous variables were described with means while categorical variables were described with absolute numbers and percentages. The incidence was calculated using simple proportions. Means were compared using students t test and Fishers exact for variables with cells less than 5. Correlation between continuous variable was assessed using Pearson correlation.

3. RESULTS AND DISCUSSION

3.1 Results

Samples were accepted from 436 newborns. (this included 5 set of twins and therefore 431 mothers).

Out of the 436 newborns, 51.4% were females. There was a female to male ratio of 1.06:1. The mean birth weight (± 2 standard deviation) is 3.3 ± 1.4 kg. Out of the total, 375 (86%) of the newborns had an appropriate birthweight while 33 (7.6%) had low birthweight and 28 (6.7%) were large for gestational age with a birthweight above the 90^{th} percentile. The mean length (±2SD) was 48.1±4.4 cm with a range of 33 to 53 cm. The head circumference had a mean (±2SD) of 34.6 ±.2 cm with a range of 22 to 38 cm.

The biochemical features of the neonates are as follows.

The mean (±2SD) cord blood TSH level was 7.09 ±5.17 mIU/L with a range of 1.0 to 32.0 mIU/L Out of the 436 subjects, 27 (6.2%) of them had increased TSH levels defined as ≥ 15 mIU/L with a mean of 23.01 mIU/L. While those below the cut-off were 409(93.8%) and had a mean of 6.02 mIU/L.

The cut off used for screening was 15 mIU/L. There was no statistically significant difference between the mean weight, length and head circumference of those with increased and normal levels of TSH. Increasing maternal age or weight of the babies did not have a direct relationship with increasing values of TSH. (γ =0.006 and -0.038)

Free T_4 assay was performed on these twenty-seven and six of them were found to have a low value lower than 0.8ng/dl which is lower than the lower limit of the reference range (0.8-2.0 ng/dl). Twenty-one [21] of them had hyperthyrotropinaemia. While [6] 1.4% were found to have congenital hypothyroidism.

The sex ratio among the neonates with CH was 1:1. None of the neonates with CH had a birth weight that was small or large for gestational age.

A higher frequency of mothers of neonates with CH were aged 35 years and above (33.3%) in relation to the age of mothers of neonates without CH. (15.3%).The frequency of insecticide use was similar in both groups of mothers (30% versus 33%). The frequency of mothers that made use of iodized salt was similar in both groups. No risk factor showed any statistical significance.

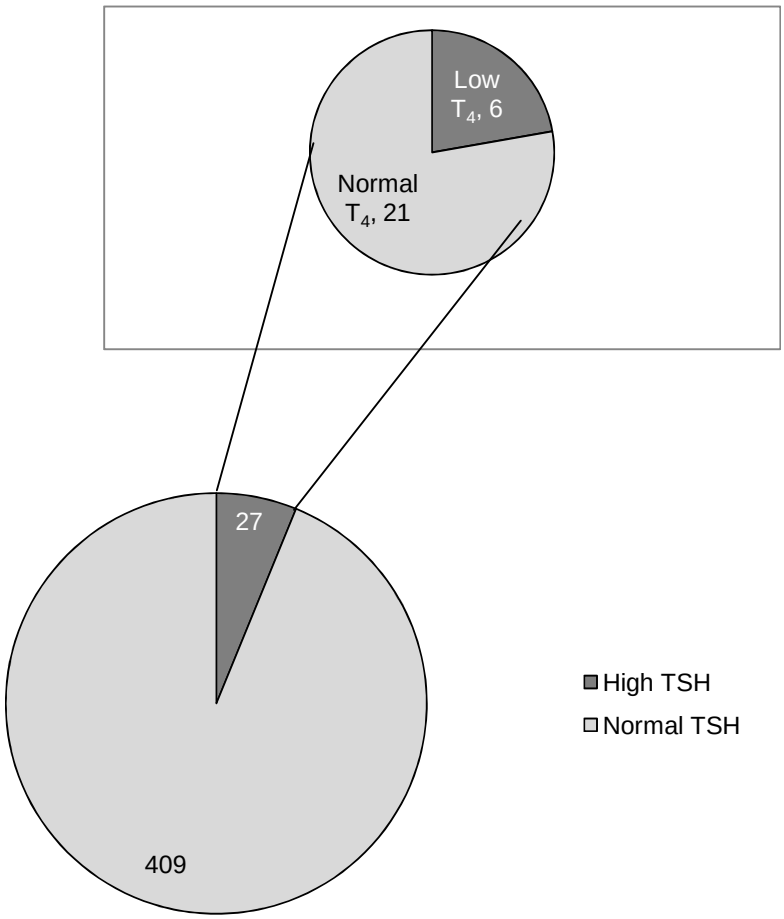

Fig. 1. Biochemical diagnosis of congenital hypothyroidism

Table 1. A comparison of the physical characteristics of those with congenital hypothyroidism and those without congenital hypothyroidism (N =436)

Variable	Neonates with CH	Neonates without CH	*P*-value
Weight (kg)	3.30±0.36	3.3±1.4	0.9530
Length (cm)	49.17±2.32	48±4.5	0.5566
Head circumference (cm)	35.50±2.17	34.6±2.1	0.3143

Table 2. Characteristics of the mothers (N=436)

Variable	Frequency	%
Age		
<20	3	0.7
20-24	46	10.6
25-29	154	35.3
30-34	165	37.8
35+	68	15.6
Marital status		
Married	432	99.1
Single	2	0.5
Cohabiting	2	0.5
Education		
Primary	14	3.2
Secondary	163	37.4
Tertiary	259	59.4
Religion		
Christianity	432	99.1
Islam	4	0.9
History of consanguinity		
No	436	100
Yes	0	0
Use of iodized salt		
No	106	24.3
Yes	330	75.7
Type of gestation		
Singleton	426	98.0
Twin	10	2.0

The six newborns were recalled and their TSH and free T_4 measured. They were also examined at one month of age for neurological defects such as hypotonia and signs of hypothyroidism such as an enlarged tongue, umbilical hernia and hoarse cry. At this time, it is expected that the elevated TSH levels will be physiologically below 10mIU/L and any elevation at this stage will definitely be pathological. At one month of age their TSH and free T_4 were found to be within normal limits. The value used for confirmation of a diagnosis of CH is 10 mIU/L

The mean age of the mothers was 30.0 (±) 4 years with a range of 17 to 44 years. Most of the mothers were married. There was no history of consanguinity. None of the twins in the study had congenital hypothyroidism.

The thyroid profile of the mothers of the six recalled newborns was done and all parameters (TSH, free T_4 and free T_3) were within the reference range.

3.2 Discussion

In the present study, the mean TSH was 6.04 mIU/L and this was comparable to the 5.95 mIU/L reported in a study done in Sokoto in Northern Nigeria but much higher than the 1.86 mIU/L reported in a multicentre study done in Nigeria [25]. The present study made use of the protocol that is more commonly used worldwide [26].

The frequency of increased cord blood TSH (≥15 mIU/L) in this study was 6.2%. This is lower than the 11.5% found in India by Gupta [27]. These neonates are said to have hyperthyrotropinaemia defined as the presence of increased levels of TSH with normal levels of T_4 [3].

The frequency of CH in this study was found to be 1.4%. This value is close to that found in Saki, Western Nigeria where a prevalence of 1.5% [10] was reported. It is lower than that reported in Jos (3.8%) and Bassa, (16.4%) [11] both in Plateau State. Jos is not within the iodine deficient area of Nigeria, and it has a prevalence more than 200% higher than that found in UPTH. (Port Harcourt is not located in the iodine deficient belt of Nigeria) Bassa is known as an area with endemic iodine deficiency [11] and thus the markedly increased prevalence is not surprising. Most of the infants in Bassa had a reversal of biochemical findings to euthyroid states after the first few weeks of life. The frequency of CH obtained in UPTH is comparatively higher than that in a province in South Africa with a value of 0.1% [28] and that in Austria at 0.03% [29].

Among the six newborns that had CH there were no clinical features at birth suggestive of congenital hypothyroidism such as, poor muscle

tone, rough facial features and an enlarged tongue.

These neonates were recalled for a follow up visit and four of them returned at four weeks postpartum. At this time, it is expected that the elevated TSH levels will be physiologically below 10mIU/L and any elevation will definitely be pathological. A repeat estimation of serum TSH and free T_4 was done for them. At this second visit, they were examined by a Paediatrician and their motor development was adequate for their age. The weight, length and head circumference of three out of four of the infants were adequate for the age of the children. The fourth, a female had all parameters at the 90th percentile.

These four infants had a biochemical hypothyroid picture at birth but by one month of age they were euthyroid. A diagnosis of transient primary congenital hypothyroidism was made [3]. This is defined as hypothyroidism present at birth that resolves usually within the first four to six weeks of life but sometimes persists up to a year and may require treatment [30]. These four infants would not require treatment as they have had a reversal of biochemical features.

The mean age of the mothers (± 2SD) in this study was 30.0 ±4.5 years. Some studies have found that increasing maternal age has an effect on increasing value of TSH in cord blood [31]. Although this study found an increased frequency of CH among the older mothers, this association was not statistically significant.

Seventy six percent of the mothers made use of iodized salt. This is very likely the effect of the iodinization program instituted at the World Summit for Children in 1990. Port Harcourt is a sea port town that is close to salt water and has many salt water tributaries. Fish and other sea food make up a regular part of the diet of the people. Therefore it is not expected that the residents of Port Harcourt would be iodine deficient. There is no statistical difference between the use of iodized salt in mothers of babies with CH and those without. This is in keeping with what is expected in sporadic congenital hypothyroidism.

4. LIMITATIONS

The use of TSH in making a diagnosis of hypothyroidism does not identify hypothyroidism due to secondary causes. Therefore secondary hypothyroidism which is very rare would have been missed.

Some mothers were not interested in taking part in the study due to personal reasons or cultural beliefs.

5. CONCLUSION

The prevalence of transient primary congenital hypothyroidism in this study was 1.4%. This is higher than that found in most parts of the world and similar to studies done previously in Nigeria. At birth there was no clinical feature to distinguish between those with congenital hypothyroidism and those without. The mothers of these hypothyroid babies were euthyroid and there was no risk factor described.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors. All authors confirm that informed consent was obtained from all participants in the study.

ETHICAL APPROVAL

Ethical approval was obtained from the ethical committee of the University of Port Harcourt Teaching Hospital prior to the start of the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Delange F. Screening for congenital hypothyroidism used as an indicator of the degree of iodine deficiency and of its control. Thyroid. 1998;8(12):1185-1192.
2. Hashemipour M, Dehkordi EH, Hosseiny L. Outcome of congenital hypothyroid screening program in Isfahan, Iran from prevention to treatment. Int J Prev Med. 2010;1:92-97.
3. Rose SR, Brown RS. Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics. 2006;117: 2290-2303.
4. Hinton CF, Harris KB, Borgfeld L, Drummond-Borg M, Eaton R, Lorey F, et al. Trends in incidence rates of congenital hypothyroidism related to selected demographic factors: Data from the United States, California, Massachusetts, New

York and Texas. Pediatrics. 2010;125: 537-547.
5. Onyiriuka AN, Abiodun PO, Onyiriuka LC. Thyroid disorders in childhood and adolescence. Pac J Med Sci. 2012;10:3-11.
6. Ibekwe MU, Ibekwe RC, Okolo AA, Cheetham TD. Screening for hypothyroidism in schools for children with learning difficulties in South-eastern Nigeria. J Trop Pediatr. 2013;59:330-331.
7. Hashemipour M, Dehkordi EH, Hosseiny L. Outcome of congenital hypothyroid screening program in Isfahan, Iran from prevention to treatment. Int J Prev Med. 2010;1:92-97.
8. Tarim O. Thyroid hormones and growth in health and disease. J Clin Res Pediatr Endocrinol. 2011;3:51-55.
9. Porterfield SP. Vulnerability of the developing brain to thyroid abnormaliites: Environmental insults to the thyroid system. Environ Health Perspect. 1994;102:125-130.
10. Ojule AC, Osotimehin BO. Maternal and neonatal thyroid status in Saki, Nigeria. Afr J Med Sci. 1998;27(1-2):57-61.
11. Das SC, Isichei UP, Otokwula AA, Emokpae MA, Mohammed AZ. Neonatal chemical hypothyroidism in Nigeria. Ann Trop Paediatr. 2004;24(3):237-240.
12. Toublanc JE. Comparison of epidemiological data on congenital hypothyroidism in Europe with those of other parts of the world. Horm Res. 1992;38:230-235.
13. Donaldson M, Jones J. Optimising outcome in congenital hypothyroidism, current opinions on best practise in initial assessment and subsequent management. J Clin Res Pediatr Endocrinol. 2013;5:13-22.
14. Ugboma HAA, Onyearugha CN. Still births in a tertiary hospital, Niger Delta area of Nigeria; Less than a decade to the millennium developmental goals. Int J of Trop Dis Health. 2012;2:16-23.
15. George IO, Jeremiah I. Perinatal outcome of babies delivered to eclamptic mothers: A prospective study from a Nigerian tertiary hospital. J Biomed Sci. 2009;5(4):390-394.
16. Deladoey J. Congenital hypothyroidism due to thyroid dysgenesis: From epidemiology to molecular mechanisms. In: Springer D (editor). A new look at hypothyroidism. Intech Rijeka, Croatia. 2012;229-239.
17. Buyukgebiz A. Newborn screening for congenital hypothyroidism. J Clin Res Pediatr Endocrinol. 2013;5:8-12.
18. Adeniran KA, Okolo AA, Onyiriuka AN. Thyroid profile for appropriate for gestational age neonates in Nigeria: A fore runner to screening for congenital hypothyroidism. J Trop Pediatr. 2010;56(5):329-332.
19. Afroze B, Humayun KN, Qadir M. Newborn screening in Parkistan- lessons from a hospital-based congenital hypothyroidism screenings programme. Ann Acad Med Singapore. 2008;34(12):114-116.
20. Lebea PJ, Pretoria PJ. Newborn screening for classic galactosaemia and primary congenital hypothyroidism in the Nkangala district of the Mpumalanga province of South Africa. S Afr J Child Health. 2008;2(1):19-22.
21. Mak PPY, But WM, Yu CM, Chow CB, Li KY, Lee LP, Yam WKL, Tse PWT, Fung E, Lau J, Tse WY. Thyroid dysfunction in Chinese children and adolescents with Down's syndrome. Hong Kong J Paediatr. 2006;11:110-117.
22. Mengreli C, Kanaka-Gantenban K, Girgimoudis P, Magiakou MA, Christalopoulou L, Giannoulia-Karantana A, et al. Screening for congenital hypothyroidism: The significance threshold limit in False-Negative results. J Clin Endocrinol Metab. 2010;97(5):4283-4290.
23. Mehari A, Challa F, Gebreyesus G, Alemayehu D, Seifu D. Establishment of reference intervals of thyroid function tests from cord blood of neonates in two selected hospitals, Addis Ababa, Ethiopia. BMC Pediatr. 2016;16:118-120.
24. Fuse Y, Wakae E, Nemob Y, Uga N, Tanaka M, Maeda N, et al. Influence of perinatal factors and sampling methods on TSH and thyroid hormone level in cord blood. Endocrinol Japonican. 1991;38(3): 297-301.
25. Yahere IE, Jaja T, Oduwole A, Ibekwe MU, Suwaid S, Alkali Y, et al. Normative thyroid stimulating hormone values for healthy Nigerian newborns. Horm Res Paediatr. 2016;85(1):22-28.
26. Leger J, Olivieri A, Donaldson M, Torresani T, Krude H, Van Vliet G, et al. European Society for paediatric endocrinology consensus guidelines on screening, diagnosis and management of congenital hypothyroidism. J Clin Endocrinol Metab. 2014;99(2):363-384.

27. Ugege MO, Airede KI, Jiya NM. Thyroid function profile in cord blood and post natal changes at 24 and 72 hours in healthy term Nigerian neonates. Niger J Paed. 2014;41(3):209-214.
28. Armanian AM, Hashemipour M, Esnaashari A, Kelishadi R, Farajzadegan Z. Influence of perinatal factors on thyroid stimulating hormone level in cord blood. Adv Biomed Res. 2013;2:48-50.
29. Bijarna S, Wilcken B, Wiley VC. Newborn screening for congenital hypothyroidism in very-low-birth-weight babies: The need for a second test. J Inherit Metab Dis. 2011;34:827-833.
30. Bhavani N. Transient congential hypothyroidism. Indian J Endocrinol Metab. 2011;15:117-120.
31. Mockute I, Svedas E, Raskauskiene N, Mickuviene N, Bunevicius R. The new born thyroid stimulating hormone levels in relation to maternal age and gestation at birth. Lietuvos Akušerija Ir Ginekologija. 2010;13(3):278-284.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/18295