Newborn Screening for Congenital Hypothyroidism in Khon Kaen University Hospital, the First Three Years, A Preliminary Report

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Abstract

Between January 2000 and December 2002, 9,558 of 10,868 live births at Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand, were screened for congenital hypothyroidism (CH). Dried blood spot thyroid stimulating hormone (TSH) was collected at age 48 hours or older. The cut-off TSH level for recall test was > 25 mu/L. Serum thyroxine (T4), Free T4 and TSH were performed during the confirmatory test. Six of 24 infants recalled for confirmatory thyroid function tests had abnormal tests. Primary CH was confirmed in 3 infants and thyroxine treatment was given. Two of the three infants had thyroid dysgenesis, one had normal thyroid gland. Three infants showed borderline CH from the confirmatory test, only one had borderline CH from the second confirmatory test and also received thyroxine treatment. Twenty infants with false positives during the screening and confirmatory tests were regularly followed-up for growth, development and thyroid function tests. The incidence of primary CH in this sole tertiary care government hospital in Northeast Thailand was 1 : 3,186. Routine newborn CH screening would ensure early detection and treatment.

Key word : Congenital Hypothyroidism, Newborn Screening, Borderline Hypothyroidism, Thailand

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Newborn screening was first developed in America by Guthrie in 1960-1961[1]. In 1973-1974, Dussault in Canada demonstrated that dried blood on a filter paper could be used as a screening tool for congenital hypothyroidism (CH)[2]. Thereafter, Europe and North America instituted nation-wide CH screening. Japan, Hong Kong, Taiwan, Singapore, Australia and New Zealand also have nation-wide screening. Worldwide incidence of CH is about 1 : 3,500 but it is much higher in iodine-deficient areas and among certain population groups[3]. The first newborn CH screening project in Thailand was performed by Sukthomya between 1982 and 1986[4]; subsequently, most Thai hospitals perform CH screening. The incidence of CH in Thailand varies between 1 : 2,500 and 1 : 6,000[5-10]. Srinagarind Hospital, Khon Kaen University the sole university and government tertiary hospital in Northeast Thailand, cooperated with the Ministry of Public Health to do CH screening since January 2000. The authors report the incidence of CH in infants born at Srinagarind Hospital. The establishment of baseline incidence will guide therapeutic interventions forestalling mental retardation and developmental disabilities in affected children.

MATERIAL AND METHOD

Blood thyroid stimulating hormone (TSH) levels were determined in newborns delivered at Srinagarind Hospital for a 3-year period between January 2000 and December 2002. The filter - paper spot TSH and phenylketonuria screening tests were performed in collaboration with the Ministry of Public Health Program. Heel-prick dried blood samples were collected by medical students from infants aged 48 hours or more. Radioimmunometric assay was used to measure the TSH level with a cut-off of 25 mu/L for patient recall and further evaluation. Re-evaluation consists of complete physical examination and repeated blood tests for serum thyroxine (T4), Free T4, and TSH by radioimmunoassay using commercially available kits (ICN Biomedicals, Inc. CA, USA), performed at RIA laboratory unit, Srinagarind Hospital. CH was indicated if clinical and repeated blood test showed abnormal serum T4, TSH and Free T4. Bone age determination and thyroid scan were performed and levothyroxine treatment was initiated. Borderline hypothyroidism was indicated when only the confirmatory serum TSH was elevated (between 5 and 10 mu/L) and serum T4 and Free T4 were normal. Thyroid function test was repeated 4 weeks later.

The Ethical Committee of the Faculty of Medicine, Khon Kaen University, approved the protocol and informed, written consent was obtained from the parents. Failure to obtain informed parental consent constituted exclusion from the study. Premature (< 37 weeks gestation) infants and those whose mothers had thyroid diseases were excluded..

Descriptive statistics were used : percentages for the coverage, recall, and response rate while the incidence rate was the number of cases per total screened during the study.

RESULTS

Between January 1, 2000 and December 31, 2002, 9,558 of 10,868 live births at Srinagarind Hospital, Khon Kaen University, Khon Kaen, were screened for CH (Table 1). Screening coverage averaged 87.95 per cent. Twenty-six infants were recalled for re-evaluation establishing a recall rate of 0.27 per cent. Twenty-four of the 26 infants (92.31% response rate) had a confirmatory blood test for serum T4, TSH and Free T4. Abnormal confirmatory tests were found in six infants, only three (one occurred each year) had clinical and laboratory findings indicative of CH (Table 2). The incidence of CH in the present study was therefore 1 : 3,186. Two of the three infants had

Table 1. Number of infants with TSH screening, coverage, recall, response rates, and infants with congenital hypothyroidism (CH) at Srinagarind Hospital during January 2000 to December 2002.

Year	Number of infants								
	Livebirths	Screening	Coverage (%)	Recall	%	Response	%	CH (incidence)	Borderline CH
2000	4,066	3,237	79.61	11	0.34	10	90.9	1 (1 : 3,237)	1 (1 : 3,237)
2001	3,275	2,794	85.31	7	0.25	7	100.0	1 (1 : 2,794)	-
2002	3,527	3,527	100.0	8	0.23	7	87.5	1 (1 : 3,527)	2 (1 : 1,764)
Total	10,868	9,558	87.95	26	0.27	24	92.31	3 (1 : 3,186)	3 (1 : 3,186)

widened fontanels, and one in three showed clinical jaundice and dry skin. Two infants had thyroid dysgenesis and one had normal thyroid judging from ultrasonography and scintigraphy. Three infants had borderline hypothyroidism, with normal T4, Free T4, and mildly elevated serum TSH (i.e. between 5 and 10 mu/L) without clinical symptoms of CH. Thyroid function test was followed-up 4 weeks later. Two infants had normal TSH levels four weeks after follow-up. One had serum TSH > 5 mu/L (Table 3), but normal thyroid gland and bone age, so thyroxine was initiated at age 70 days. During the study period, there were four infants from mothers with Graves disease and received propylthiouracil treatment. All had a high level of screening TSH but normal confirmatory thyroid function test.

The screening- TSH reported by the Ministry of Public Health using 13 to 45, 20 to 60 and 12 to 33 days for the first, second and third year, respectively. None had positive tests for phenylketonuria.

DISCUSSION

During the three-year study only 6 of 24 infants had an abnormal confirmatory thyroid function test. Three infants had abnormal serum T4, Free T4 and TSH confirmatory test. The incidence of overt

Table 2. Clinical and laboratory findings of infants with congenital hypothyroidism from newborn screening of 3 year period.

Clinical and laboratory findings	Congenital hypothyroidism		
	Infant 1	Infant 2	Infant 3
Sex	Female	Male	Male
Birthweight (g)	2,710	3,120	3,520
Widen fontanels	+	-	+
Dry skin	-	+	-
Jaundice	-	-	+
Screening TSH (mu/L)	35.91	> 160.16	58.12
Serum T4 (μg/dl)	4.0	4.10	4.10
TSH (mu/L)	25.3	> 48	44.32
Free T4 (ng/dl)	0.9	0.6	0.8
X-ray bone age	Normal	Normal	Normal
Ultrasonography of thyroid gland	Normal	Absent	Single lobe thyroid gland
Thyroid scan	Normal	No uptake	Single lobe thyroid gland
Age at treatment (days)	27	45	25

Table 3. Clinical data and thyroid function test of 3 infants with borderline hypothyroidism.

Clinical and thyroid function test	Infant 1	Infant 2	Infant 3
Sex	Male	Male	Female
Birthweight (g)	3,030	2,790	3,060
Screening TSH (mu/L)	29.11	28.49	27.41
Confirmatory test 1			
T4 (μg/dl)	9.24	9.92	8.51
TSH (mu/L)	5.06	6.94	6.62
Free T4 (ng/dl)	1.47	1.28	1.02
Confirmatory 2 (after 4 weeks)			
T4 (μg/dl)	11.02	11.18	9.25
TSH (mu/L)	3.16	2.86	5.54
Free T4 (ng/dl)	1.53	1.20	1.19
X-ray bone age	-	-	Normal
Ultrasonopraphy of thyroid gland	-	-	Normal gland
Thyroid scan	-	-	Normal gland
Age at treatment (days)	-	-	70

CH among newborns screened in our hospital was 1 : 3,186, which is comparable to the national incidence in Thailand[6-9]. Perhaps because of the low birth rate, only one case of CH occurred per year. Diagnosis of primary CH was not difficult to establish, so thyroxine was initiated at age 25 to 45 days. There were another three infants with borderline screening results and again at their subsequent confirmatory tests but all were asymptomatic and had normal serum T4, Free T4 with TSH levels, between 5 to 10 mu/L. It is quite difficult to distinguish this group of infants from those who have true hypothyroidism and therefore need to be treated. Some reports withheld treatment and continued monitoring these patients, postulating that the hypothyroid is transient and will resolve with time[11,12]. A German study reported abnormalities of TSH level in only three of 61 school children with transient or borderline CH during the newborn period with normal growth and development[12]. In an American study of 13 borderline CH who received thyroxine therapy for 3 years, found 10 of the 13 children had abnormal TSH levels after the therapy was discontinued at 3 years of age. Three had normal TSH and underwent thyrotropin releasing hormone (TRH) test : two had an abnormal response to TRH [13]. An exaggerated TSH response to TRH stimulation test was found in 7 of 43 infants with borderline hypothyroidism in another study[14]. A recent Italian study demonstrated significantly higher basal serum TSH in children between 16 and 44 months of age who had false positive or borderline CH at their newborn screening and confirmatory examination when compared to the control group. Moreover, these infants had a higher prevalence of antithyroid antibodies, frequent thyroid morphology abnormalities, frequent thyroperoxidase and TSH receptor gene sequences variations[15]. Very little data demonstrate the long-term outcome for infants with mild or mininal evidence of hypothyroidism. Three studies from different areas found some children with transient or borderline hypothyroidism had physical, mental and/or psychomotor developmental delays[16-18]. In the present study,18 infants had false positive results on the newborn screening test and normal recall or confirmatory test. Two infants had an abnormal first confirmatory test but was normal for the second test and have regular follow-up for thyroid function test, growth and development to avoid either over-treatment or under-treatment.

Inadequate personnel for newborn screening at our hospital is a major limitation so blood samples were collected by the fifth and sixth year medical students on rotation in the newborn ward. Interns and residents carried out the screening tests four weeks of the year the ward was not served by medical students. Coverage has improved to a response rate of 92.31 per cent. Wrong addresses and no telephone access limited follow-up to two mothers and their children. Ignorance of the screening test on the part of the parents and a lack of cooperation from medical personnel were encountered.

The authors conclude that routine newborn CH screening in Thailand is necessary for early detection and treatment. Educating parents and health workers of the importance of screening would improve the response rate, communication and monitoring. Newborn testing and subsequent monitoring should be offered free-of-charge.

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การคัดกรองภาวะพร่องไทรอยด์ฮอร์โมนในทารกแรกเกิด ในโรงพยาบาลศรีนครินทร์, คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น, ผลการศึกษา 3 ปีแรก

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ระยะเวลา 3 ปี ระหว่างเดือนมกราคม 2543 ถึงเดือนธันวาคม 2545 มีทารกแรกเกิดมีชีวิตจำนวน 10,868 คน ที่โรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ทารกจำนวน 9,558 คนได้รับการตรวจคัดกรองภาวะพร่องไทรอยด์ฮอร์โมน โดยการเจาะเลือดดู TSH จากส้นเท้า หยดบนกระดาษซับและทำให้แห้งในขณะที่เด็กอายุ 48 ชั่วโมง หรือมากกว่า ทารกที่มีซีรั่ม TSH ผิดปกติ คือ ระดับมากกว่า 25 mu/L จะถูกเรียกตัวกลับมาตรวจระดับซีรั่ม T4, Free T4 และ TSH ทารก 6 ใน24 คนที่ถูกเรียกตัวกลับมาครั้งแรกมีระดับเลือดผิดปกติ โดย 3 ใน 6 คนมีระดับซีรั่ม T4, Free T4 และ TSH ผิดปกติ 2 ใน 3 คนนี้พบมี dysgenesis ของต่อมไทรอยด์ 1 คนมีต่อมไทรอยด์ปกติ ทั้ง 3 คนได้รับการรักษาด้วยไทรอยด์ฮอร์โมน อุบัติการณ์ของภาวะพร่องไทรอยด์ฮอร์โมนเท่ากับ 1 : 3,186 ทารกอีก 3 คนพบระดับ TSH สูงเล็กน้อย โดยที่มีระดับ T4 และ Free T4 ปกติ การตรวจการทำงานของต่อมไทรอยด์ซ้ำครั้งที่สอง พบ 1 ใน 3 ยังมีระดับ TSH สูงเล็กน้อย จึงได้ให้การรักษาด้วยไทรอยด์ฮอร์โมน ทารกที่มีผลการตรวจการทำงานไทรอยด์เป็นผลบวกลวง จำนวน 20 คนยังคงได้รับการติดตามการเจริญเติบโต, พัฒนาการ และการทำงานของต่อมไทรอยด์อย่างสม่ำเสมอ จากการศึกษานี้พบว่าการคัดกรองภาวะพร่องไทรอยด์ฮอร์โมนในทารกแรกเกิดในประเทศไทยยังมีความจำเป็นเพื่อค้นหาผู้ป่วยใหม่และให้การรักษาให้เร็วที่สุดเท่าที่จะทำได้

คำสำคัญ : ภาวะพร่องไทรอยด์ฮอร์โมนแต่กำเนิด, การคัดกรองในทารกแรกเกิด, ภาวะพร่องไทรอยด์ฮอร์โมนแบบไม่ชัดเจน, ประเทศไทย

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