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(Citation)

The Kobe journal of the medical sciences, 37(6):265-271

(Issue Date)

1991

(Resource Type)

departmental bulletin paper

(Version)

Version of Record

(URL)

<https://hdl.handle.net/20.500.14094/E0034256>



THYROID FUNCTION IN NEWBORN INFANTS FROM GOITROUS AND NON GOITROUS MOTHERS

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INDEXING WORDS

thyroid function ; newborn ; goitrous mothers ; iodine deficiency disorders (IDD) area

SYNOPSIS

Endemic goiter is one of the health effects of iodine deficiency. Enlargement of the thyroid is often seen during pregnancy especially in the endemic iodine deficiency disorders (IDD) areas. Thyroid hormones have a vital role in the fetal development and maturation of the brain. The lack of these hormones may result in neurological damage.

We measured thyroid hormones and TSH in cord blood and TSH in newborn's blood from dry blood spots on filter paper in 5-14 th days, from 58 non goitrous and 61 goitrous mothers. T4, T3 and TSH concentrations in cord blood were measured by enzymeimmunoassay (EIA) using enzymum test Boehringer and TSH from dry blood spots on filter paper were measured by radioimmunoassay (RIA). Goiter size was graded as follows : O, I, II and III.

There were significant differences in cord serum T3 concentrations between non goitrous and goitrous mothers with grade I, II and III. TSH concentration in newborn's blood from goitrous mothers of grade III were significantly higher than those from non goitrous mothers and from goitrous mothers of grade I. T4 concentration in cord blood from non goitrous mothers in IDD area was significantly lower than those from non IDD area and those from goitrous mothers in the IDD area. There were significant differences also between TSH concentration in newborn's blood spots from goitrous mothers in IDD area and those from goitrous mothers in non IDD area and from non goitrous mothers in IDD area. Two cases of congenital hypothyroidism were found in infants from goitrous

Received for publication : December 26, 1991

Authors' names in Japanese : スナルティニ, 中村 肇

mothers. This paper explains the fact that newborns from goitrous mothers especially in severe iodine deficient areas could accompany with abnormal thyroid function.

INTRODUCTION

About six million people are suffering from endemic goiter of various stages in Central Java Indonesia, and women are more likely to have a chance of having endemic goiter than men. In several previous studies the prevalence of goiter was much greater in females than in males (Hersman, JM. et al 1983) and in certain area 80% of endemic goiter cases are women. Thyroid enlargement is also demonstrable in the majority of pregnancies especially in the Iodine Deficiency Disorders (IDD) areas. Before 1974, the prevalence of cretinism is 7-13% in IDD areas. A goiter accompanied with hypothyroidism may cause spontaneous abortion, congenital goiter or cretinism. Thyroid function of neonate is independently from the thyroid function of mother, however the hypothyroid infants born from hypothyroid mothers can be often found in the very severe IDD areas. Our previous study in Yogyakarta indicated that the incidence of congenital hypothyroidism in neonates were one in around 1,500 (Sunartini et al. 1990). It is also difficult to establish early diagnosis of congenital hypothyroidism, since a clinically mild hypothyroidism is not easily detected, and the interpretation of biochemical data is not well known in the presence of iodine deficiency. This study has been conducted to examine the thyroid function of newborn infants from goitrous and non goitrous mothers in the IDD areas.

MATERIALS AND METHODS

Third trimester pregnant women who had her antenatal care in the health centers or district hospital in Yogyakarta Province were examined for goiter. Sixty one goitrous pregnant women and 58 non goitrous were serially examined for antenatal care. Thyroid size were graded according to Perez, C. et al (1960) as follows :

Grade of goiter		thyroid examinations
Grade	O	Not palpable and not visible (normal)
Grade	I a	Palpable more than one thumb large but not visible
	b	Palpable more than one thumb large and visible if neck elevated
Grade	II	Palpable and visible in normal position
Grade	III	Goiter visible from a distant

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Cord blood were collected by birth attendants, midwives or doctors who helped delivery. The sera were frozen and stored at -20°C . T₄, T₃ and TSH were measured by enzymeimmunoassays using Enzymum test Boehringer. TSH of newborn was also measured by Radioimmunoassay (Corning Amersham RIA) using dry blood spots on filter paper at Central Laboratory, Hyogo Medical College Japan. Dry blood spots on filter paper were collected by heel puncture between 5 and 14 days after birth and were stored in refrigerator before mail.

All data were analysed using Macintosh Statwork program for descriptive analysis and Student's t tests. The data are expressed in mean $\pm$ SD .

RESULTS

One hundred and nineteen cord sera (61 samples from goitrous mothers and 58 from non goitrous) were examined for T₄, T₃ and TSH. Gestational age were 38.8 ± 1.2 weeks for non goitrous mothers and 38.8 ± 4.3 weeks for goitrous mothers. Birth weight were 2996 ± 544 grams for non goitrous mothers and 3134 ± 411 grams for goitrous mothers. Two infants with congenital hypothyroidism were excluded.

Table 1 : Thyroxine, triiodothyronine and thyrotropin concentration in cord sera and thyrotropin concentration in newborn's sera according to goiter size of the mother

Parameters	Grade of goiter size			
	Gr. 0 n= 58	Gr. I n= 42	Gr. II n= 14	Gr. III n= 3
Cord sera				
T ₄ ($\mu\text{g}/\text{dl}$)	7.2 ± 3.2	7.6 ± 2.6	8.4 ± 2.3	6.1 ± 4.5
T ₃ (ng/dl)	40 ± 11	49 ± 21	78 ± 39	70 ± 26
TSH ($\mu\text{U}/\text{ml}$)	6.9 ± 3.9	6.3 ± 4.5	7.1 ± 5.3	5.7 ± 3.9
Newborn's blood spots				
TSH ($\mu\text{U}/\text{ml}$)	2.2 ± 1.4	3.5 ± 2.5	4.1 ± 2.3	9.2 ± 10

No significant differences in cord serum T₄ and TSH concentrations were found among the subjects grouped according to goiter size. There were significant differences in cord serum T₃ concentrations between non goitrous and goitrous mothers of grade I ($p < 0.05$) and of grade II and grade III ($p < 0.001$, $p < 0.001$).

There were also significant differences in TSH concentrations in newborn's blood from goitrous mothers of grade III compared with those from non goitrous mothers ($p < 0.001$) and from goitrous mothers of grade I ($p < 0.05$) (Table 1)

Table 2. The incidence of low T4, low T3, high TSH in cord blood and high TSH concentration in newborns from IDD and non-IDD areas

Parameters	Non-IDD area n = 49		IDD area n = 70	
	n	%	n	%
Cord blood				
Low - T4 < 5.0 $\mu\text{g/dl}$	4	8.2	20	28.6*
Low - T3 ≤ 20 ng/dl	1	2.0	3	4.3
High-TSH $\geq 20\mu\text{U/ml}$	0	0	4	5.7
Newborn's blood				
High-TSH > 10 $\mu\text{U/ml}$	0	0	5	7.1

* $p < 0.01$ by chi-square test

In table 2, twentyfour infants showed T4 level lower than 5.0 $\mu\text{g/dl}$, 4 from non IDD area and 20 from IDD area ($p < 0.01$ by chi square test). Four infants had very low concentrations of T3 (20 ng/dl) , and 4 infants showed TSH concentrations in cord blood higher than 20 $\mu\text{U/ml}$. Five infants had high concentrations of TSH in newborn's blood and two infants out of them showed very high concentration of TSH. These infants born to goitrous mothers of grade I and III were diagnosed congenital hypothyroidism. Laboratory data of these cases are as follows:

Case 1 : cord blood T4 : 1.0 $\mu\text{g/dl}$, T3: 20 ng/dl, TSH : 40 $\mu\text{U/ml}$ and TSH from dry blood spot was higher than 150 $\mu\text{U/m}$. *Case 2* : cord blood T4 : 1.3 $\mu\text{g/dl}$; T3 : 30 ng/dl ; TSH 40 $\mu\text{U/ml}$ and TSH in dry blood spot was 21 $\mu\text{U/ml}$.

Cord serum concentrations of T4, T3 and TSH in goitrous and non goitrous mothers from IDD and non IDD areas are shown in table 3. T4 concentrations in cord serum from non goitrous mothers in IDD area were significantly lower than those from non goitrous mothers in non IDD area ($p < 0.001$), and those from goitrous mothers in the IDD area ($p < 0.001$). There were significant differences in T3 concentrations of cord blood between goitrous and non goitrous mothers in both IDD ($p < 0.001$) and non IDD areas ($p < 0.05$) and there were significant differences also between the concentrations of T3 in cord blood from goitrous mothers in IDD ($p < 0.05$) and non IDD areas ($p < 0.05$) .

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Table 3 : Thyroxine, triiodothyronine and thyrotropin concentrations in cord sera and thyrotropin concentration in newborn's sera from goitrous and non goitrous mothers in IDD and non IDD areas

Parameters	Non goitrous mothers		Goitrous mothers	
	N.IDD area	IDD area	N.IDD area	IDD area
Cord sera	n = 29	n = 29	n = 20	n = 39
T4 ($\mu\text{g/dl}$)	9.0 $\pm$ 2.0	5.4 $\pm$ 2.5	7.8 $\pm$ 2.8	8.0 $\pm$ 2.3
T3 (ng/dl)	40 $\pm$ 13	41 $\pm$ 8.8	48 $\pm$ 7.7	63 $\pm$ 36
TSH ($\mu\text{U/ml}$)	6.6 $\pm$ 2.7	7.3 $\pm$ 4.8	6.5 $\pm$ 4.3	6.5 $\pm$ 4.8
Newborn's blood spots				
TSH ($\mu\text{U/ml}$)	2.1 $\pm$ 1.7	2.3 $\pm$ 0.9	2.1 $\pm$ 1.1	4.6 $\pm$ 2.7

There were no significant differences in TSH concentrations in cord blood from both groups of mothers in IDD and non IDD areas. TSH concentrations in newborn's blood from goitrous mothers in IDD area were higher than those in newborns from non goitrous mothers in the same IDD area ($p < 0.001$) and from goitrous mothers in non IDD area ($p < 0.001$).

DISCUSSION

Although thyroid function of the infant is independent from maternal thyroid function (Fisher,D.A.,1986) , an iodine deficiency of pregnant women will influence thyroid metabolism in the fetus. The offspring from mother with severe iodine deficiency may suffer from neurological damage. Both gestational age and birth weight can be affected also by nutrition or abnormal thyroid function of their mothers (Sava,L. et al 1984), however there were no differences between the neonates from goitrous and non goitrous mothers except two goitrous mothers delivered premature babies.

The normal T4 and T3 concentrations in cord blood from these goitrous mothers were considered as the effect of iodine supplementation during pregnancy. In this study T3 concentrations in cord blood were higher in goitrous than in non goitrous subjects. In general the concentrations of T3 in cord blood were very low compared with the concentration in adult. The very low cord T3 levels found in this study similar with most previous reports (Fisher,D.A.,1986).

TSH concentrations in newborn's blood from goitrous mothers in the IDD areas were significantly higher than those from the other groups of infants. In previous studies high level of TSH in newborns in the IDD areas correlates with the high incidence of transient hypothyroidism in newborn (Sava, L. et al 1984). In this study we couldn't find a typical case of iodine deficiency disorders, because of mass iodized salt and iodized oil injection program intervention. This program decreased the incidence of endemic goiter and endemic cretinism (Gaitan, E. et al. 1989, Goslings, B.M. 1977). We found two cases of primary congenital hypothyroidism with low T4 level and high TSH level both in cord serum and in newborn's blood, in contrary with the other previous study in Central Java Indonesia (Dulberg, et al cit. Tuchinda, C. 1988) where no cretinism were identified amongst children after 1974. This study has important public health implication, because it has been revealed that in these areas cases of congenital hypothyroidism or cretinism born from goitrous mothers are still present. In our previous study of neonatal screening for congenital hypothyroidism in Yogyakarta Indonesia, the incidence of congenital hypothyroidism was one in around 1,500, that is, 2-5 times higher than in other countries (Sunartini, 1990) and iodine deficiency strongly considered as one of the risk factors causing congenital hypothyroidism. The findings of normal thyroid function in most of these infants further substantiates the adequacy of the mass iodization program. On the other hand the fact that babies suffer from cretinism still present in this area supported our consideration that iodized salt and iodized oil injection program for preventing endemic goiter and endemic cretinism in Indonesia should be reevaluated more deeply and should be followed by neonatal screening for cretinism.

ACKNOWLEDGEMENT

We wish to thank our colleague and the staff in Trisnowati, Turi and Ngaglik Health Centers in Yogyakarta Province, for providing samples of cord blood, to our colleague in Dept. of Pediatrics Kobe University School of Medicine especially Dr. Toshikazu Takahashi, Dr. Toru Takumi and Dr. Hisahide Nishio for their laboratory joint work, to Prof. Akira Matsuoka and Dr. Yoshiki Sato in Hyogo Medical College for performing the TSH dry blood spots measurements and to JSPS and ICMR Kobe University for the financial support.

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