*Original Article*

# THYROID FUNCTION IN MOTHERS WHO GAVE BIRTH TO NEONATES WITH TRANSIENT CONGENITAL HYPOTHYROIDISM

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**ABSTRACT**

*Objective:* To determine the thyroid status of mother's of newborns with primary congenital hypothyroidism.

*Methodology*: Thyroid function tests were carried out on 80 mothers of hypothyroid newborns and 80 mothers of non-hypothyroid newborns as control.

*Results*: The mean difference of the tests revealed that mothers of congenitally hypothyroid infants had a lower triiodothyronine resin uptake (T3RU) concentrations compared with the control population. The higher value of free thyroxin index (FTI) in case group showed a tendency to significance. The proportional frequency distribution showed; T3RU and triiodothyronine (T3) had a significant difference, and FTI showed a tendency to significance. There were no significant differences between; thyroid-stimulating hormone (TSH), thyroxine (T4) and anti-thyroid peroxidase antibodies (anti-TPO) in two groups.

*Conclusions*: These results indicated that at least some cases of primary congenital hypothyroidism were attributable to the maternal thyroid disease. Therefore, we recommend that each pregnant woman should be assessed for thyroid function in region with a high prevalence of thyroid disease.

**KEY WORDS:** Congenital hypothyroidism, Thyroid function tests, Anti-thyroid peroxidase antibodies, Mother's thyroid status.

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## INTRODUCTION

During pregnancy, the thyroid is subjected to stresses and undergoes several adaptations to maintain sufficient output of thyroid hormones for both the mothers and fetus.[1] Thyroid diseases in pregnancy are a group of disorders with different clinical manifestations, requiring a rational approach in their diagnosis and management.[2] The syndrome of transient congenital hypothyroidism is caused by: inappropriate concentration of human chorionic gonadotropin (HCG) in plasma, mutation and / or resistance to the thyrotropin-releasing hormone receptor and changes in titers and the biological action of thyrotropin hormone receptors antibodies.[3] The cause of more than 80% of thyroid disorder is autoimmunity in which antibodies are produced against

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thyroid tissue. These antibodies are IgG often, which are able to pass through placenta and induce transient congenital hypothyroidism in newborns.[4]

The prevalence of thyroid autoimmune disease during the gestational age has been reported to be highly variable: 5.2% in Belgium and 12.5% in north America.[5] Anti-thyroid peroxidase antibodies (anti-TPO) were detected in mothers of infants with transient congenital hypothyroidism, 20% and 43% in Canada and India, respectively.[6] However, some reports did not reveal the high percentage of cases with congenital hypothyroidism and thyroid antibodies.[7,8] It has been known that, availability of maternal thyroxine (T4) is needed for the developing brain in fetus and it's only source of thyroid hormone during the first trimester; T4 is the required substrate for the ontogenically regulated generation of triiodothyronine (T3) in the amounts needed for optimal development in different brain structures.[9] Endemic goiter is one of the health problems in many countries including Iran[10] and Pakistan.[11] About 70% of the total population in Pakistan is at risk of iodine deficiency disorder. The overall prevalence of congenital hypothyroidism is 1/500to 1/1000 and it was concluded that incidence of CH may be higher in children born to mothers of Pakistani, Indian and Bangladeshi origin.[11] However incidence of CH were reported 1/2500 to1/2800 in India[12] and 1/1504 in Sri Lanka.[13]

From 1988 national iodized salt consumption program has been started in Iran and since then almost all people have routinely and effectively used this salt.[14] In the 1990 survey, more than 50% of children had elevated serum thyroid-stimulating hormone (TSH) values in some parts of Iran. Screening of 4000 newborns in Tehran showed a transient elevation of TSH in 20%.[15] Also, a study in Fars province (south-east of Iran) indicated a transient congenital hypothyroidism in 7.3% and permanent in 1 to 423.[16] A recent screening study in Isfahan showed permanent incidence of 3.1/1000 live birth.[17] In the other study on 16000 newborns in Tehran, these values were 1.4% and 1 to 950, respectively.[18] Our previous study in Rafsanjan (middle of Iran) indicated a much higher frequency of transient congenital hypothyroidism, 24.2%.[19]

This study was planned to evaluate the possible association of transient congenital hypothyroidism in newborns with mothers' thyroid function tests including anti-TPO antibody of mothers.

## METHODOLOGY

Eighty mothers of transient congenital hypothyroid neonates' (neonates' TSH >20mU/L) and 80 mothers of non-hypothyroid newborns (neonates' TSH <20mU/L) were selected within 1 to 3 months post partum in 2004. Five ml of fasting blood from each participants were taken in the morning. Serum was separated and thyroxine (T4), triiodothyronine (T3), triiodothyronine resin uptake (T3RU) were determined using RIA kits ( Kavoshyar Iran), TSH by IRMA kit (Kavoshyar Iran) and anti-peroxidase (Anti-TPO) by ELISA kit (IBL, Germany). Based on the reference values of the kits each parameter's value was recorded. The data were then analyzed using independent T test and Chi Square test for quantitative variables, and $P<0.05$ was considered as significant. The study was approved by the Ethical Committee of the Rafsanjan University of Medical Sciences.

## RESULTS

The T test analyses of the mean differences of triiodothyronine resin uptake (T3RU), T3, T4, TSH, free thyroxin index (FTI) and anti-peroxidase (Anti-TPO) revealed that the mothers of congenitally hypothyroid infants had a lower T3RU concentrations compared with the control population ($p=0.000$) and higher value of FTI in case group showed a tendency to significance ($p=0.080$). These differences were not observed for the values of the other parameters (Table-I).

The Chi Square test analyses of the proportional frequency distribution showed; T3RU and T3 had significant differences ($p = 0.050$ and $p = 0.030$ respectively) and FTI showed

Table-I: The comparative values of mean and standard error (SE) for thyroid function tests. Thyroid-stimulating hormone (TSH), thyroxine (T4), triiodothyronine (T3), triiodothyronine resin uptake (T3RU), free thyroxin index (FTI), anti-peroxidase (Anti-TPO).

| *Group* | *TSH (mIU/L)* | *T3RU(%)* | *T3( nmol/L)* | *T4 (nmol/L)* | *FTI (%)* | *Anti-TPO (IU/ml)* |
|---|---|---|---|---|---|---|
| Case | 8.48 ± 5.16 | 32.14± 0.48 | 6.09 ± 2.75 | 114 ± 5.23 | 2.91 ± 0.14 | 1539.0 ± 1254.6 |
| Control | 2.46 ± 0.44 | 35.58± 0.35 | 1.64 ± 0.13 | 117.5 ± 4.42 | 3.23 ± 0.12 | 35.4 ± 4.4 |
| P value | 0.249 | 0.000 | 0.109 | 0.656 | 0.080 | 0.234 |

Mean±SE

tendency to differences (p=0.055) between two groups. In case group, 15% (n=12) had low, 83.8% (n= 67) normal and 1.3% (n=1) high T3RU versus 5% (n=4), 90% (n=72) and 5% (n=4) in control group, respectively. Twelve point five percent (n=10) of individuals in case group showed a high level of T3, 86.3% (n=69) were normal and 1.3% (n=1) had a low level of T3. These values for control group were 2.5% (n =2), 86.3% (n =69) and 11.3% (n = 9) respectively. Regarding FTI in case group, 10% (n=8) had low, 60% (n=48) had normal and 30% (n=24) had high values, while in control group these values were 1.3% (n=1), 67.5% (n=54) and 31.3% (n=25), respectively. There were no significant differences between; TSH, T4 and Anti-TPO in two groups (P= 0.216, P= 0.422 and P= 0.295, respectively). A summary of results is shown in Table-II.

## DISCUSSION

Congenital hypothyroidism occurs in 1 in 4000 neonates and is one of the most frequent preventable causes of mental retardation. In approximately 10% of babies detected by screening, the thyroid dysfunction will be transient.[20] Medical researchers have recently begun their studies on the possible etiological role

Table-II: The proportional frequency distribution of thyroid-stimulating hormone (TSH), thyroxine (T4), triiodothyronine (T3), triiodothyronine resin uptake (T3RU), free thyroxin index (FTI) and anti-peroxidase (Anti-TPO) in case and control groups.Normal range: TSH (0.3-4mIU/L), T3RU (30 -40%), T3 (1.05 - 3.2nmol/L), T4 (60 – 150nmol/L), FTI (1.5 – 3.6%) and Anti-TPO (>100 IU/ml: high, 50 – 100 IU/ml: borderline and <50 IU/ml: normal)

| *Parameter* | *Status* | *Case n (%)* | *Control n (%)* | *Total n (%)* | *P value* |
|---|---|---|---|---|---|
| TSH | High | 6 (7.5%) | 6 (7.5%) | 12 (7.5%) | 0.216 |
| | Normal | 71 (88.8%) | 74 (92.5%) | 145 (90.6%) | |
| | Low | 3 (3.8%) | 0 (0.0%) | 3 (1.9%) | |
| T3RU | High | 1(1.3%) | 4 (5%) | 5 (3.1%) | 0.050 |
| | Normal | 67 (83.8%) | 72 (90%) | 136 (86.9%) | |
| | Low | 12 (15%) | 4 (5%) | 16 (10%) | |
| T3 | High | 10 (12.5%) | 2 (2.5%) | 12 (7.5%) | 0.003 |
| | Normal | 69 (86.3%) | 69 (86.3%) | 138 (86.3%) | |
| | Low | 1 (1.3%) | 9 (11.3%) | 10 (6.3%) | |
| T4 | High | 12 (15%) | 12 (15%) | 24 (15%) | 0.422 |
| | Normal | 61 (76.3%) | 65 (81.3%) | 126 (78.8%) | |
| | Low | 7 (8.8%) | 3 (3.8%) | 10 (6.3%) | |
| FTI | High | 24 (30.0%) | 25 (31.3%) | 49 (30.6%) | 0.055 |
| | Normal | 48 (60.0%) | 54 (67.5%) | 102 (63.8%) | |
| | Low | 8 (10%) | 1 (1.3%) | 9 (5.6%) | |
| Anti-TPO | High | 7 (8.8%) | 5 (6.3%) | 12 (7.5%) | 0.295 |
| | borderline | 2(2.5%) | 0.00 | 2 (1.3%) | |
| | Normal | 71 (88.8%) | 75 (93.8%) | 147 (91.2%) | |

in some of these transient cases of maternal TSH receptor-blocking antibodies.[21] A high frequency of family history of goiter and / or hypothyroidism has been reported among both permanent and transient congenital hypothyroidism infants.[22] In this study, we investigated and compared the thyroid function in mothers of neonates with transient congenital hypothyroidism and of neonates with normal thyroid function.

Our results showed, mean difference of T3RU in transient congenital hypothyroidism neonates' mothers were lower compared to normal thyroid neonates' mothers, hence mothers of hypothyroid newborns had more hypothyroid disorders. The absolute and proportional frequency distribution showed; T3RU and T3 had a significant difference (p= 0.050 and p= 0.030 respectively) however, FTI showed a tendency to significance (p=0.055). Physiologic changes associated with pregnancy require an increased availability of thyroid hormones by 40% to 100% in order to meet the needs of mother and fetus during pregnancy. In the first trimester of gestation, the fetus is wholly dependent on thyroxin from the mother for normal neurologic development.[9] Any maternal iodine deficiency results in a range of intellectual, motor, and hearing deficits in offspring.[23] Goiter is endemic in some countries. The main cause of endemic goiter is iodine deficiency. Endemic goiter in Iran has been attributed primarily to compensatively iodine deficiency, and that following all salt factories added iodine to their product to diminish the detrimental effects of iodine deficiency from 1988.[14] Iranian people have had consumed iodized salt for many years, but goiter appears in different shapes.[14,16,18] There is evidence that iodine induced thyroid dysfunction and autoimmunity among population with endemic goiter.[24] Anti-TPO are the hallmark of autoimmune thyroid disease and are present in almost all patients with Hashimoto's thyroiditis, in two-thirds of patients with postpartum thyroiditis and also in 75% of patients with Graves' hyperthyroidism.[25] Although mean difference of anti-TPO was found 1539.0 ± 1254 in case group against 35.4 ± 4.4 in control group (Table-I) and absolute and proportional frequency distribution of anti-TPO showed; in 8.8% (n = 7) high and 2.5% (n = 2) borderline in case group versus only 6.3% (n = 5) in control group and these differences were not significant (Table-II), but it is not enough to judge that how is its role in the high prevalence of transient congenital hypothyroidism in this area.

On the other hand, thyroid secretion increases during pregnancy in normal women, because of the need to provide thyroid hormones to their fetus and because the women's own needs. Women with marginally low thyroid function before pregnancy are less likely to be able to meet these needs.[26] T4 is converted in peripheral tissues to bioactive T3 by thyroxine-5'-deiodinase enzyme. Many non-thyroidal illnesses (such as; stress , chemical exposure , free radical load, liver disease, kidney disease, toxic metal exposure and….) are associated with inhibition of 5'-deiodinase activity in peripheral tissues, resulting in a decrease of circulating bioactive T3.[27] Probably these non-thyroidal illness affect both case and control groups, but its effect on control population (normal thyroid neonates' mothers) showed decrease of T3 less than limited normal range as it was not seen in transient congenital hypothyroidism neonates' mothers.

## CONCLUSIONS

We suggest a global strategy for the systemic screening of thyroid function during pregnancy, based on an algorithm that allows for the diagnosis of both autoimmune and non autoimmune forms of thyroid disorders in the pregnant state for people who live in endemic goiter area.

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