Original Article

Higher TSH levels in the first trimester of pregnancy are related to lower birth weight

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Abstract. To determine whether there was an association between birth weight and maternal thyroid function in the early first trimester.

Early first trimester thyroid stimulating hormon (TSH) levels and birth weight percentiles of pregnants attending to our outpatient obstetrics clinic were searched retrospectively.

Mothers of infants with small for gestational age (SGA) infants had statistically significantly higher mean TSH values when compared to mothers of infants with appropriate for gestational age (AGA) and large for gestational age (LGA) infants (2.5±8 and 1.7±1.5 respectively, p=0.007). Also, mothers of infants under 2500g weight had higher TSH values in the first trimester when compared to mothers of infants over 2500g weight (2±0.8 and 1.8±1.6 respectively, p=0.045).

There was an association between high TSH levels in the early first trimester and low birth weight, screening of thyroid functions and treatment before pregnancy might be considered as a better policy.

Key words: TSH, small for gestational age, birth weight

1. Introduction

Decreased function of the thyroid gland during pregnancy may increase the risk of obstetrical complications (1,2) and may affect the neuropsychological development of the child in the early postnatal life (3,4). Overt hypothyroidism affects 0.3-0.5% and subclinical hypothyroidism affects 2-3% of the pregnant women (5). Most of the patients with hypothyroidism are asymptomatic or have symptoms mimicking those of pregnancy. Screening pregnant women according to targetted high-risk criteria was reported to miss one third to one half of the pregnant women with hypothyroidism when compared with screening everyone for thyroid disease during pregnancy (6,7).

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The association between hypothyroidism and growth retardation in childhood is well established (8). The aim of the present study was to evaluate whether the early first trimester maternal thyroid stimulating hormon (TSH) levels affected birth weight or not.

2. Materials-methods

This was a retrospective study performed by searching the data of women attending to our outpatient obstetrics clinic for their routine first pregnancy visit between January 2006 and April 2011. All patients with an intrauterine pregnancy and fetal cardiac activity confirmed with ultrasound and with blood tests including TSH between the 6th and 8th weeks of pregnancy were included. The patients were grouped according to neonatal birth weights. Maternal serum concentrations were measured by an immunoassay using direct chemoiluminometric technology (Roche Diagnostics, GMBH Mannheim). The lowest limit for a detectable TSH concentration was 0.005mU/L. All of the patients with increased TSH levels were retested and levels of free T4, free T3 and thyroid autoantibodies were measured. All of the patients with abnormal thyroid functions were consulted by an endocrinologist and achieved euthyrodism

in the second trimester and reached the previously suggested upper limit of TSH in the first trimester of pregnancy, 2.5mU/L or second trimester of pregnancy, 3mU/L (9). None of our patients received iodine supplementation before or during pregnancy. We did not check the iodine levels. Only the patients delivering in our institute after the 34th week of pregnancy were included. Study protocol was in confirmation with the ethical guidelines of the Declaration of Helsinki.

Exclusion criterias were pregnancies with incomplete information, known abnormal fetal karyotype, congenital malformations, multiple pregnancy, maternal illnesses as hypertension and preeclampsia, gastrointestinal malabsorption and also smoking. We did not exclude any case on the basis of abnormal fetal biometry or birth weight. We did not take the gender of the fetus and the method of conception into consideration.

Small for gestational age (SGA) was defined as below and equal to the 10th percentile and large for gestational age (LGA) was defined as above and equal to the 90th percentile for that gestational age and other infants were defined as appropriate for gestational age (AGA) as defined for Turkish population previously (10). Gestational age was calculated according to the last menstrual period confirmed by the first trimester crown-rump length measurement.

For statistical analysis we used NCSS (Number Cruncher Statistical System) 2007 and PASS (Power Analysis and Sample Size) 2008 statistical Software (Utah, USA). Data showing anthropometric parameters were presented as mean±standard deviation. Data showing normal distribution of parameters were compared with Student's t-test, data showing non-normal distribution of parameters were compared with Mann Whitney U test. Within 95% confidence interval p values <0.05 were considered as statistically significant. The results were considered statistically significant when the p-value was calculated less than 0.05 at a confidence interval of 95%.

3. Results

We included 554 patients in our study. The demographic features of the patients were shown in Table 1.

Table 2 shows TSH levels, where mothers of SGA infants had statistically significantly higher mean TSH values in the first trimester when compared to mothers of AGA and LGA infants (2.5±8 and 1.7±1.5 respectively, p=0.007). Also mothers of infants born < 2500g (n=16) had higher TSH values in the first trimester when compared to mothers of infants born ≥2500 g (n=538) (2±0.8 and 1.8±1.6 respectively, p=0.045).

In the receiver operating curve (ROC) analysis, area under the curve for infants <2500 g determined the cut-off value as 0.616 (SE 0.039, p=0.007). TSH values above 1.65 had a sensitivity of 69%, specificity of 54%, positive predictive value of 4% and negative predictive value 98% in predicting low birth weight infants.

Table 1. Demographic features of the patients

(n=554)	Range	Mean ±SD	Median
Age (years)	19-43	30±4	30
Gravidity	0-6	1.5±0.9	1.00
Parity	0-3	0.3±0,5	0.4
Maternal weight before pregnancy (kg)	40-104	62.5±10	60
Maternal weight at delivery (kg)	56-117	78±11	77
Maternal weight gain in pregnancy (kg)	-2 to 45	15±5	15
Gestational age at TSH measurement (weeks)	6-8	7.2±1	7.1
Maternal height at delivery (cm)	150-180	164±5.8	161
Gestational age at delivery (weeks)	34- 42	38.9±1	38.8
Birth weight (grams)	1640-4900	3380±453	3400
Birth weight percentile (%)	1-100	48±27	47
TSH (mU/L)	0.04-28.60	1.8±1.6	1.57

TSH: Thyroid stimulating hormone
SD: standard deviation

Table 2. Thyroid stimulating hormone (TSH) levels

		TSH (mU/L)		p
		Mean ±SD	Median	
Birth weight percentile	SGA (n=9)	2.5±8	1.96	0.007**
	AGA-LGA (n=545)	1.7±1.5	1.52	
Birth weight (g)	< 2500 (n=16)	2±0.8	2.13	0.045*
	≥ 2500 (n=538)	1.8±1.6	1.55	

Mann Whitney U Test *p<0.05, **p<0.01
SD: standard deviation
SGA: Small for gestational age
AGA: Appropriate for gestational age
LGA: Large for gestational age

4. Discussion

This study documented that pregnancies delivering SGA neonates had higher TSH levels in the early first trimester. Previously performed studies searching for the effects of thyroid dysfunction on pregnancy were performed after 11th week of pregnancy when most of the miscarriages had already occurred (1,11-13). When the aim is to ameliorate the adverse maternal and fetal effects due to thyroid dysfunction, than early diagnosis and treatment will benefit from screening more. A recently published study showed three times increased of low-birth weight neonates with high first trimester TSH levels (14). All of our patients underwent treatment and achieved euthyroidism in the second trimester, despite this patients with higher TSH levels in the early first trimester had lower birth weight infants. This may be the result of a mechanism acting earlier, at the time of the trophoblastic invasion. Thyroid hormone transporters are present in the placenta throughout the gestation, their expression may affect transplacental thyroid hormone passage from the mother to the fetus and may lead to abnormal placentation (15,16). Abnormal placentation was the proposed mechanism for the delivery of SGA neonates (17,18). This may be the explanation for the association between increased maternal TSH values in the early first trimester and SGA infants in our study. Increasing TSH was associated with an increasing risk of child loss in early pregnancy, including pregnants with TSH levels in the normal range (2). Therefore screening and therapeutic intervention before pregnancy might be a better policy.

In the first trimester of pregnancy serum TSH levels are supressed by the elevated circulating human chorionic gonadotropin concentrations (5). Human chorionic gonadotropin was reported to have a transient thyrotropic effect and very rarely it caused TSH concentrations to be suppressed below the nonpregnant reference interval (19). Our study revealed an increased risk of SGA with increasing TSH values even when it is in the normal range. Previously performed studies reported that there was no difference between mean birth weight of infants with normal maternal thyroid hormones and thyroid dysfunction (1,20,21). On the contrary a lower mean birth weight was reported in infants of pregnants with increased TSH levels (11,21-23). TSH levels were also reported to be higher in neonates that had lower birth weight (23,24). These findings may be further supportive for prepregnancy screening and treatment. Treatment of low risk patients with thyroid disorders was shown to be beneficial (25,26). Screening of thyroid function abnormalities during pregnancy by determination of serum TSH levels was also shown to be cost-effective (27,28).

A limitation of our study was the retrospective nature of it. We did not take thyroid hormone concentrations, thyroglobulin antibody levels and thyroid peroxidase antibody levels into consideration. Another shortcoming of the study was that we were not able to consider the iodine deficiency, the most common cause of hypothyroidism in pregnancy. Blacksea region of Turkey has known endemic goiter due to dietary habits, but this study was not performed in that region and the policy of iodine supplementation in daily salts was shown to eliminate hypothyroidism due to iodine dficiency in Turkey.

In conclusion there was an association between high TSH levels in the early first trimester and low birth weight, screening of thyroid functions and treatment before pregnancy might be considered as a better policy.

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