

Thyroid Dysfunction Prevalence in a Turkish Pregnant Women Population Living in Black sea Region

Senol Senturk^{1*} and Nilgul Akalin²

¹Faculty of Medicine, Department of Obstetrics and Gynecology, Erdogan University, Rize, Turkey

²Department of Internal Medicine and Nephrology, Konuk Training and Research Hospital, Istanbul, Turkey

*Corresponding author: Senol Senturk, Faculty of Medicine, Department of Obstetrics and Gynecology, Recep Tayyip Erdogan University, Islampasa, Sehitler Street, Turkey Tel: +90 464 2170370; E-mail: dr.senturk@hotmail.com

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Abstract

Background: We have aimed to determine thyroid dysfunction prevalence among pregnant women in a city of Black Sea Region that iodine deficiency is most frequently seen in our country.

Materials: We have included pregnant women in their 7-8 days to 12th weeks of gestation according to last menstrual cycle. Serum triiodothyronin, tetraiodothyronin, thyroid stimulating hormone and anti-thyroperoxidase levels were measured.

Results: We have observed that iodine deficiency seen in the region did not have any effect on maternal thyroid dysfunction prevalence. Maternal thyroid dysfunction prevalence was not different from maternal thyroid dysfunction prevalence reported in the worldwide. There was no statistically significant difference between prevalence of hyperthyroidism and hypothyroidism.

Conclusion: Thyroid dysfunction prevalence should be established in all regions especially among pregnant women population. Thus, frequently seen cases of endemic goitre, endemic cretinism and fetal maternal complications in last 3-4 decades could be prevented.

Keywords: Iodine deficiency; Pregnancy; Thyroid dysfunction; Prevalence

Introduction

It is known that maternal goitre development risk is increased especially in regions that iodine deficiency is seen because of the changes in iodine metabolism and serum thyroid binding proteins during pregnancy. It was demonstrated that some immunological changes such as shift of T-helper-1 lymphocytes to T-helper-2 lymphocytes contribute to maternal goitre development [1]. Effects of serum thyroid hormone levels on central and peripheral nervous system development has become a research subject especially in last 10 years. Negative effect of low serum maternal thyroxin levels on fetal IQ development during pregnancy is counted among the factors that made maternal thyroid dysfunctions important [1].

It is accepted that thyroid functions should be followed starting from early pregnancy in first trimester as it is known that thyroid dysfunctions might cause preterm deliveries and abortion in addition to severe hyperemesis gravidarum. Maternal thyroid dysfunctions are documented as hypothyroidism, hyperthyroidism, subclinical hypothyroidism, and subclinical hyperthyroidism and hypothyroxinemia presentations.

According to the results of some researches, thyroid dysfunction might develop in one of every six pregnant women in iodine deficiency regions. It is reported that the real reason for hyperthyroidism which develops during pregnancy could be Graves' disease and chorionic

gonadotropin related hyperthyroidism toxic multinodular or toxic nodular goitre [2,3].

The results of recent studies detected that maternal hyperthyroidism could be seen in 5 of every 1000 pregnant women and 1.29 of 1000 cases of hyperthyroidism have gestational antidrug use history [4,5]. Study results showed that risk of maternal hyperthyroidism is increased and medication used for the treatment could be the reason of fetal complications other than maternal hepatic toxicity [2,6].

It is also observed in other studies that neonatal intensive care necessity and preterm delivery risk is increased in infants in case of maternal hyperthyroidism however congenital malformation risk is decreased. It is observed that iodine deficiency is an important factor for the aetiology of maternal thyroid dysfunctions and severe disorders such as endemic goitre, hypothyroidism and cretinism, endemic mental deficit, cognitive deficit could develop.

It is detected that iodine deficiency plays a role in development of maternal hypothyroidism and maternal hypothyroidism could be seen about 50% rates in case of iodine deficiency and 25-30% of these cases develop permanent hypothyroidism [1,7]. Hypothyroidism incidence in pregnant population is detected as 3-10 cases per 1000 pregnant women generally [7].

We have aimed to detect effects of regional iodine deficiency on maternal thyroid functions in addition to detect the maternal thyroid dysfunction prevalence by evaluating thyroid functions in first trimester of pregnancy in Rize province, which is known as endemic

iodine deficiency region, of Black Sea Region with a population of 300,000.

Materials

The study is conducted including pregnant women admitted to Recep Tayyip Erdogan University Research and Training Hospital Obstetrics and Gynaecology Clinic during 2013-2015. Recep Tayyip Erdogan University Research and Training Hospital Ethical Committee approved the study and each of the cases included in the study was informed in detail and informed consent was received.

A total of 534 pregnant females aged 18-47 were included in the study. The objective is to determine the thyroid dysfunction prevalence among pregnant females during first trimester (7-8 days to ≤ 12 weeks of gestation calculated from the last menstrual cycle). Therefore, patients with a history of a disease (Rheumatoid arthritis, psoriatic arthritis, etc.) or a medication (carbamazepine, valproic acid, Coumadin, lithium, cortisone, etc.) that could affect thyroid hormone levels were not included.

Acute or recent upper respiratory tract infection cases that could increase the risk of subacute thyroiditis, cases with thyroid operation history, cases that are applied methimazole, carbimazole, propylthiouracil and L-thyroxine to regulate thyroid functions and pregnancies >13 weeks of gestation were not included. Ages and gestational weeks of the pregnant females included in the study had been recorded and venous blood samples were collected following 12 hours fasting to evaluate thyroid dysfunctions and serum TSH and anti-TPO levels were measured with the same device under the same circumstances.

Venous blood samples had been transferred to the laboratory prevented from hemolysis and centrifuged at 4°C at 2500 xg for 10-15 minutes and wait in the cold chain. Biochem immunosystem brand 96 tests commercial test kits had been used for serum Thyroid Stimulating Hormone (TSH) level measurements. Serum TSH and anti-thyroid peroxidase antibody levels were evaluated with immunoassay method (Access[®] Immunoassay kits, Beckman Coulter UniCel DXI 800). Normal ranges were assumed as 0.27-4.2 uIU/ml for serum TSH and as 1-35 IU/ml for anti-thyroid peroxidase (anti-TPO) antibodies and anti-TPO levels >35 IU/ml had been evaluated as antibody positivity.

Results

About 534 pregnant females aged 18-47 were included in the study. Age distribution of all women included in the study was 18-49 and mean age was 32.01 ± 5.99 years. Mean serum TSH level was 1.60 ± 0.90 uIU/ml and mean anti-TPO level was 25.66 IU/ml.

Serum TSH levels of 224 of 534 pregnant women were between normal ranges recommended for pregnancy (TSH: 0.27-2.50 uIU/ml) and mean age of these cases was 33.11 ± 5.50 years and mean serum TSH levels was 1.24 ± 0.40 uIU/ml and mean anti-TPO levels was 27.00 IU/ml.

Serum TSH levels of 15 out of 534 cases (2.80%) were measured >4.20 uIU/ml and accepted as thyroid dysfunction (hypothyroidism). Mean age of these cases was 34.26 ± 6.66 years mean serum TSH level was 6.187 ± 2.54 uIU/ml and mean anti-TPO was 28.00 IU/ml (Table 1).

Variables	Euthyroid pregnancy (n=501)	Hypothyroid pregnancy (n=15/2.80%)	Hyperthyroid Pregnancy (n=18/3.37%)	P
Mean Age (year)	32.01 ± 0.15	34.26 ± 6.66	32.01 ± 5.50	0.2
Thyroid Stimulating Hormone (IU/ml)	1.502 ± 0.85	6.187 ± 2.54	0.119 ± 0.99	0.01
Antithyroid-peroxidaz (IU/ml)	24	28	25	0.3

Table 1: Evaluation of thyroid functions among pregnant women [$p < 0.05$].

Serum TSH levels of 18 cases out of 534 (3.37%) were below 0.27 uIU/ml and accepted as thyroid dysfunction (hyperthyroidism). Mean age of these cases was 32.01 ± 5.50 years and mean serum TSH level was 0.119 ± 0.99 uIU/ml and mean anti-TPO level was 25.00 IU/ml. Mean age, serum anti-TPO levels were not significantly different ($p > 0.05$) in hypothyroidism and hyperthyroidism cases however serum TSH levels were significantly different ($p < 0.05$) (Figure 1) (Table 2).

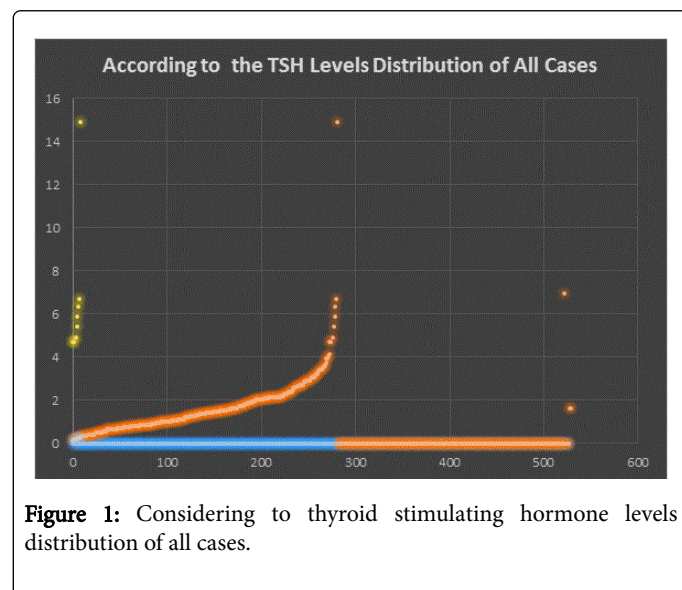


Figure 1: Considering to thyroid stimulating hormone levels distribution of all cases.

Variable	Euthyroid pregnancy women	Hypothyroid pregnancy women	Hyperthyroid pregnancy women
Age (years)	0.216	0.289	0.833

Table 2: Evaluation of influences of age on thyroid functions in pregnancy women.

No statistically significant difference was observed when the mean age and serum anti-TPO levels of cases with thyroid and target TSH levels (TSH: 0.27-4.20 uIU/ml and TSH: 0.27-2.50 uIU/ml; respectively) were compared to mean age and anti-TPO levels of hypothyroid and hyperthyroid cases ($p > 0.05$). Statistically significant difference was observed between serum TSH levels ($p < 0.05$) (Figure 1). Effects of mean ages of pregnancy women were not determined to

cases with euthyroid, hypothyroid and hyperthyroid ($p=0.216$; $p=0.289$; $p=0.833$; respectively) (Table 2).

Statistical Analysis

Statistical analysis was accomplished on a personal computer by using statistical program for social sciences version 11.5 (SPSS 11.5, demo, SPSS Inc. Chicago, Illinois). Mean median, 2.5th and 97.5th percentages were calculated. Kolmogorov-Smirnov test with Lillefor's correction was used to test whether the variables used in the study were normally distributed. Mann-Whitney U test was used to compare thyroid hormones, antithyroid-peroxidase, maternal ages. A p-value of <0.05 was assumed to be significant.

Discussion

Thyroid dysfunctions might cause neonatal cretinism, cognitive and mental deficits and permanent thyroid dysfunctions in postpartum period in addition to maternal and fetal complications in reproductive period. Therefore, studies are focused on thyroid dysfunctions in last 3-4 decades [8].

When thyroid physiology is investigated under normal conditions during pregnancy, it is observed that renal iodine clearance is increased, iodine transport in plasma and in placenta in the fetus is decreased, serum thyroxine binding globuline is decreased, human chorionic gonadotropins and plasma volume are decreased. As a result, it is seen that goiter develops in females with iodine deficiency, T3 (triiodothyronine) and T4 (tetraiodothyronine) increase and TSH (thyroid stimulating hormone) is decreased due to increased plasma volume and human chorionic gonadotropins [9].

Iodine deficiency is an important problem all over the world as it might cause neuro-intellectual disorders. Iodine renal clearance is increased and plasma iodine levels are decreased due to increased plasma volume and glomerular filtration rates during the first trimester of pregnancy. In this case, adaptation is tried to be achieved by decreasing intrathyroidal iodine storages and iodine renal clearance and iodine supplementation through the diet [10].

As a result of many studies, it was observed that circulating iodine concentration is not decreased in pregnant women in the regions that iodine deficiency is endemic. However, it was observed that placental iodine transportation is increased, fetal and maternal thyroid gland functions are progressively increased during the first trimester and as a result, maternal and fetal thyroid gland volumes are increased if increased need of iodine is not fulfilled [11].

Additionally, due to the physiology of thyroid gland, serum thyroid hormone changes could be detected most frequently during the first trimester and the risk of hypothyroidism in the fetus is greater during this period [12]. In summary, dietary iodine supplement to fulfil increased maternal and fetal hormone production during early pregnancy might prevent thyroid gland growth and fetal hypothyroidism, however, maternal serum iodine concentration is not effected by the iodine deficiency in the environment that the pregnant women lives.

In our study, we have aimed to determine the thyroid dysfunction incidence in a province in Black Sea Region in which endemic iodine deficiency is most commonly seen. It is reported that goiter frequency is 47.00% among females and 29.00% among males and all over goitre prevalence is 30.30% in Turkey according to a study investigating thyroid dysfunction in normal population in East Black Sea region

[13]. We have aimed to demonstrate thyroid dysfunction prevalence in our study by checking TSH levels in pregnant women during their first trimester. We have evaluated serum TSH levels as a screening test as the general opinion is that TSH levels alone could be used as a screening test for detection of thyroid dysfunctions [14].

We have measured anti-TPO antibody levels simultaneously in our cases. We have shown that hyperthyroidism frequency is higher than hypothyroidism frequency among the pregnant women that we have screened prevalence. We have seen that hypothyroidism and hyperthyroidism prevalence is similar to those reported in pregnant women in the worldwide [3,4].

It is reported that Graves' disease, thyroiditis or single or multiple toxic nodular goiter could be the reason in cases that gestational hyperthyroidism is seen. Graves' disease prevalence is about 1-3% among pregnant women and measurement of TRAbs level is recommended for diagnosis. Temporary hyperthyroidism could be seen in 5-9% of infants in maternal Graves' disease cases due to transplacental TRAbs transfer and postpartum thyroiditis risk is increased in presence of autoimmune thyroid disease, therefore the necessity of postpartum maternal and fetal thyroid function follow-up is emphasized [1,5]. Additionally, gestational hyperthyroidism treatment is accepted as an important matter that requires strict follow-up as it could cause maternal liver dysfunction and fetal congenital anomalies. We have guided the cases that we diagnosed with hyperthyroidism for differential diagnosis of Graves' disease, thyroiditis or toxic nodular goiter, treatment and follow-up.

We could not demonstrate high serum anti-TPO levels in cases that we detected maternal hypothyroidism in our study. In other studies, it was detected that positive or anti-TPO levels might affect serum thyroid hormone levels. Therefore, The United States National Academy of Clinical Biochemistry (NACB) supported determination of specific serum thyroid hormone reference intervals for each trimester according to antibody positivity or negativity. We think that false negative and positive results risk is relatively lower in our cases as we diagnosed hypothyroidism with simultaneous measurements of serum antibody levels and serum thyroid hormone levels [15,16].

In recent years, effects of age on the risk of thyroid dysfunction development has become an object for research and it was shown in a couple of cases that age does not have an effect on thyroid dysfunction development in pregnant women over 30 years or more [5]. Mean ages of all the cases thyroid, hypothyroid, or hyperthyroid are above 30 in our study, thus; we could think that age does not have an effect on thyroid dysfunction in our study as well. We have measured serum TSH levels during first trimester in our cases to determine the prevalence of gestational thyroid dysfunction and detected that maternal hyperthyroidism cases are higher than maternal hypothyroidism cases, and no significant difference was detected between their prevalence.

Different thyroid gland physiology during pregnancy and serum thyroid hormone levels most frequently seen during first trimester of the pregnancy could be the reason for higher prevalence of hyperthyroidism cases. This opinion could be supported by physiologically increased serum T3 and T4 levels and decreased TSH levels during the first trimester of pregnancy. Also, we could have been showing the presence of possible or undiagnosed autoimmune thyroid disease or toxic nodular goitre in the cases that we detected hyperthyroidism.

In summary, the reason for this result could be explained as iodine deficiency in the region is ineffective on maternal serum iodine levels and the real effective factor is the dietary iodine intake. We think that we have shown the effects of positive regulations on resources that iodine could be taken by feeding such as water and salt according to the results of prevalence study among pregnant women living in the Black Sea region.

Conclusion

It is known that the course of thyroid dysfunctions could change during pregnancy and thyroid dysfunctions might cause an increase of maternal and fetal morbidity-mortality. Thyroid dysfunctions cause maternal and neonatal complications during postpartum period and this is one of the leading reasons that it is an important health issue. We support that pregnancies should be planned and future mothers should be screened for thyroid dysfunctions.

Competing Interests

The authors have no competing interests.

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