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Evaluation of TSH level in the first trimester of pregnancy in women with no history of thyroid Disorder referred to Imam Khomeini and Razi Hospital of Ahvaz

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Abstract
Pregnancy causes physiological changes in maternal thyroid function tests and changes are occasionally confused with thyroid abnormalities, therefore the aim of this study was to determine the TSH levels in the first trimester of pregnancy in women without a history of thyroid disease. And to determine the importance of screening of thyroid diseases in early pregnancy.

Methods: This descriptive analytic study consisted of 1200 pregnant mothers in their first trimester referring to Jondishapur university hospitals for prenatal care in the span of one year. Cases with incomplete data as well as pregnant mothers with a history of thyroid disorders were excluded. In addition to routine prenatal lab test TSH level was measured by enzyme-linked immunosorbent assay (ELISA) method. It should be noted that the documented information is confidential and will not be used in any other study. All TSH measured data was analyzed by SPSS software version 26 and All P values <0.05 were considered significant.

Results: Seventy percent of our cases were aged between 25 and 35 years old. The mean age of pregnant women was 29.44±0.13 and the mean of TSH level in the first trimester of pregnancy was 2.40±0.49.There was no significant relations between different age groups, abortion, number of pregnancies and diabetes in our cases and TSH level (p>0.05). However, there was a significant correlation between BMI, family history of thyroid diseases and hypertension in pregnant women without past medical history of thyroid diseases and TSH level in the first trimester of pregnancy (p<0.05).

Conclusions: The results of this study showed that TSH level in majority of our cases ranging from 2.5 to 3.9 mUl/ml, 310(25%) cases more than 2.5 mUl/ml and 188(15.66%) cases more than 3.9 mUl/ml. According to this study approximately 16% of our cases need assessment for hypothyroidism and required treatment. If screening of TSH in first trimester was not done 188 cases of hypothyroidism would not have been diagnosed, thus it is reasonable to implement this test in the routine prenatal care.

Keywords: Thyroid disease, thyroid function tests, TSH levels, ELISA

Introduction
Pregnancies complicated by endocrine disorders such as hypothyroidism can have adverse outcomes for the mother and the fetus. The prevalence of overt and sub-clinical hypothyroidism during pregnancy was reported to be 0.2% to 0.5%, and 2% to 3%, respectively [1]. Pregnant women with hypothyroidism are at risk of several maternal complications such as preeclampsia, pregnancy induced hypertension, premature placental abruption, postpartum hemorrhage and fetal complications such as low birth and preterm labor (Before 32 weeks), however there is yet some controversy over screening for hypothyroidism in pregnancy. Some studies recommend screening during pregnancy with history of infertility [2]. It is well established that in addition to fetal thyroid hormones, maternal thyroid hormones are also essential for the normal growth of the central nervous system in the prenatal period, so the deficiency of the thyroid hormones during the prenatal period leads to irreversible brain damage [3].

Many hormonal and metabolic changes occur during pregnancy that have complex effect on thyroid hormones (The incidence of hyperthyroidism in women is about 5 in 1000 and hypothyroidism in about 3 in 1000) [4]. Due to the inexpensive nature of screening tests and treatment of overt hypothyroidism and the outcome of treatment on the fetal and maternal adverse effects screening is suggested during pregnancy [5]. Chan *et al* have shown that hypothyroidism which occurs during pregnancy can be exacerbated in postpartum period (postpartum thyroiditis) [6]. Given the significant prevalence of thyroid diseases in women of childbearing age, the prevalence of these diseases, including chronic thyroiditis, hypothyroidism, Graves' disease, etc., is also high in pregnant women [7]. Previous history of thyroid disease, a positive family history, type1 diabetes, and other autoimmune diseases or having multiple clinical symptoms suggesting thyroid problems may place a person in high risk group.

Objectives

Nowadays the importance of thyroid screening in high risk groups is well established but the usefulness of TSH testing for all women in early pregnancy is still unknown. The purpose of this study is to determine the TSH level in first trimester in pregnant women without a history of thyroid disease and to evaluate the importance of screening.

Methods

This is a descriptive analytic study on 1200 women in the first trimester of the pregnancy that referred to Imam and Razi hospital prenatal clinic for routine prenatal care in one year period, for each case a checklist was completed containing demographic information (age, weight and height), as well as the variables required for research (history of previous pregnancy, history of medical diseases and family history of thyroid disease). In addition to routine prenatal lab test TSH level was measured by enzyme-linked immunosorbent assay (ELISA) method. In the quantitative variables, the mean of the data center and the standard deviation was used to describe the scattering of data. Prevalence and percentage were used to describe the data in qualitative variables. T-test and Chi-square test were used to analyze the data. The normalization of the Kolmogorov-Smirulov test was studied. The significance level was considered to be 0.05 all analyzes were performed using SPSS software version 26.

Results

Seventy percent of women were between 25 and 35 years old and the Mean age of them was 29.7±0.13. 20% of women were younger than 25 years, % 71 of women were between 25-35 years and 8.8% of women were older than 35 years. Mean TSH level of the first Trimester was 2.4±0.04. 84.3% of pregnant women had TSH level under 3.9 mUl/ml. there was no significant relations between different age groups of pregnant women and TSH level in the first trimester of pregnancy (p>0.05).

71.66% of all cases and % 72.3 of women with normal TSH level had no history of abortion in the first trimester of pregnancy. Also there was no significant relations between abortion in pregnant women without a history of thyroid disorder and TSH level in the first trimester of pregnancy (p>0.05).

Of the 1200 pregnant women, 88.3% (1060 cases) had no family history of thyroid diseases.11.7% (140 case) had family history of thyroid disease Out of this 140 cases with family history 52 cases (37.14%) had abnormal TSH level. There was a significant correlation between family history of thyroid disease in pregnant women and TSH level in the first three months of pregnancy (p<0.05).

In the cases with normal TSH level 83.7% had two or less pregnancies and 16.3% had more than 2 pregnancies. There was no significant relations between the number of previous pregnancies and the TSH level in the first trimester of pregnancy (p> 0.05) (Table 1)

According to table 2 there is a significant correlation between BMI and abnormal TSH level (p> 0.05).

2.7% of women with TSH level under 3.9 mUl/ml had diabetes and 87.1% of pregnant women with diabetes had TSH level under 3.9 mUl/ml. 2.4% of pregnant women had hypertension. 1.8% of women with TSH level under 3.9 mUl/ml in the first trimester of pregnancy had hypertension and 62.1% of pregnant women with hypertension had TSH level under 3.9 mUl/ml Also, there was no significant relations between diabetes in pregnant women and abnormal TSH level (p> 0.05), but there was a significant correlation between high blood pressure and TSH level in the first trimester of pregnancy (p<0.05) (Table 3). The TSH level in 702 cases (58.5%) was lower than 2,5mUl/ml, in 310 cases (25.33%) were between 2.5 to 3.9mUl/ml and in 188 cases (15.66%) higher than 3.9mUl/ml. (Table 4).

Table 1: Percentage and Frequency Distribution of Demographic Variables

Statistical indicators	<3/9 Distribution(percent)	>3/9 Distribution(percent)	Total	Level of significance
Age less than 25 years	203 (20.1)	30 (16)	233 (19.4)	0.115
25-35 years	720 (71.1)	121 (64.4)	841 (70.1)	
More than 35 years	89 (8.8)	37 (19.7)	126 (10.5)	
Abortion				0.478
No	730 (72.3)	128 (68.1)	857 (71.66)	
yes	279 (27.7)	60 (31.9)	339 (28.34)	
Family history of the disease				0.000
yes	924 (91.3)	136 (72.3)	1060 (88.3)	
no	88 (8.7)	52 (27.7)	140 (11.7)	
Previous pregnancy number				0.068
2 and less than 3 pregnancies	492 (48.6)	520 (51.4)	588 (49)	
more than 2 pregnancies	96 (51.1)	92 (48.6)	612 (51)	

Table 2: Body mass index in pregnant women without a history of thyroid disorder

BMI	TSH levels during the first trimester of pregnancy Number / Percent		Total	Level of significance
	>3.9	3.9>		
Severe weight loss (less than 18.5)	0(0)	3(0.3)	3(0.3)	P=0.000
Weight loss(18.5-20)	0(0)	6(0.6)	6(0.5)	
Normal (20-24.99)	105(55.9)	575(56.8)	680(56.7)	
Overweight (25-29.9)	48(25.5)	321(31.7)	369(30.8)	
Class 1 obese(30-34.9)	20(10.6)	90(8.9)	110(9.2)	
Class 2 obese (35-39.9)	10(5.3)	12(1.2)	22(1.8)	
Class 3 obese(over 40)	5(2.7)	5(0.5)	10(0.8)	
total	188(15.7)	1012(84.3)	1200(100)	

Table 3: history of previous pregnancies in women with no history of thyroid disease in the areas

History of underlying disease		TSH levels during the first trimester of pregnancy Number/percent		Total	
		>3.9	3.9>		
Diabetes	no	184 (97.9) (15.7)	985 (97.3) (84.3)	1169 (97.4)	F=0.0228
	Yes	4 (2.1) (12.9)	27 (2.7) (87.1)	31 (2.6)	P=0.663
Hypertension	No	177 (94.2) (15.1)	994 (98.2) (84.9)	1171 (97.6)	F=10.254
	Yes	11 (5.9) (37.9)	18 (1.8) (62.1)	29 (2.4)	P=0.001

Table 4: TSH range in pregnant women

Pregnant mothers	TSH range
409(34.08)	0.03-1/5
293(24.41)	1/5-2/5
310(25.33)	2/5-3/9
188(15.66)	4-11
3/9<TSH	2/5<TSH
188	498

Discussion

The purpose of this study was to emphasize the importance of TSH screening in low risk pregnant woman.

Nazarpour *et al*. showed that the prevalence of thyroid disorders was 34.2% and among the risk factors were history of thyroid drug use, history of thyroid disorders and family history of thyroid disorders. The researchers concluded that without screening about 1/3 (35.6%) of women with thyroid disorders would not be diagnosed during pregnancy, and further study is recommended which is consistent with this study's objectives [8].

IN the study of Li C *et al*., There was a significant relationship between positive family history of thyroid disorders and the presence of thyroid disorders in pregnant women. On the other hand, this study showed that most pregnant women with thyroid disorders were aged between 20-30 years and it was found that being in this age group can be considered as an independent variable. Most of the women in this age group were in the study and were consistent with the study our colleagues [9].

Khalil AB *et al* conducted a study in emirates in which the TSH reference rate was higher than those recommended by American Thyroid Association (ATA) [10] Alexender EK in the guidelines that was published in 2017 by ATA shows that TSH level in pregnant women differs in different races, black and Asian women have TSH values lower than whites [11].

Hee-won moon in Korea designed a study and determined the normal level of TSH in each trimester0.01-4.1 for first and 0.01-4.26, 0.15-4.56 for second and third trimester respectively [12]. our study was done in Iranian population and in the first trimester. When possible ranges for serum TSH should be specified by population and gestational age.

A study done by Feki *et al*. done in pregnant women in Tunisia showed no correlation with women with diabetes melitus and thyroid disorders which is consistent with our results [13].

ATA suggests that subclinical hypothyroidism and an initial serum TSH higher than 4.5 mIU/L are at a higher probability for hypertension during pregnancy [11]. in our study we saw correlation between hypertension and abnormal TSH level.

S chen *et al*. emphasized that elevated TSH level before pregnancy was linked to increased risk of adverse pregnancy outcomes such as abortion and preterm labor regardless of using non pregnant or first trimester upper limits (4.29 mIU/L and2.5 mIU/L respectively) and they suggest considering 6 months prior to pregnancy as “pregnant status” and women ought to be observed from that time period [14].

Maraka *et al*. compared treated and untreated pregnant women with subclinical hypothyroidism and the results suggest that patients who were treated had lower probabilities of pregnancy loss especially when treated with TSH level between 4.1-10 mIU/L but not between 2.5-4 mIU/L and higher chances of preterm labor than untreated patients [15].

American College of Obstetrics and Gynecology (ACOG) does not advocate for universal screening for thyroid disease in pregnancy because the identification and treatment subclinical hypothyroidism has not been shown to prevent the adverse effect and to improve the pregnancy outcomes [16]. However according to ATA screening for thyroid diseases during pregnancy can ameliorate pregnancy outcomes, nevertheless they also suggest that subclinical hypothyroidism may not cause adverse pregnancy consequences [11].

The ACOG does not recommend treatment for subclinical hypothyroidism and advises treatment when free T4 level is low [16], but the ATA recommends evaluating pregnant women with TSH >2.5 mIU/L for the presence of Thyroid peroxidase (TPO) antibody and has categorized suggestions for the treatment of subclinical hypothyroidism based on the degree of TSH level and presence of TPO, when TPO is negative they suggest treatment with TSH level above 10 mIU/L and if TPO is positive treatment is recommended with TSH level above 4 mIU/L [11].

Conclusions

According to current national guidelines thyroid function tests are not required routinely but this study shows in 188 cases (15.6%) TSH level was above 3.9 mUl/ml. routine measurement of TSH level in first trimester is logical and if not measured 15% of pregnancies may have complications of hypothyroidism. BMI, diabetes and family history of thyroid disease were also important factors to predict high risk patients. Due to the small group of study we recommend larger and universal study to be conducted.

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