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ORIGINAL ARTICLE

Maternal Thyroid Stimulating Hormone Levels During The First Trimester Of Pregnancy At The South-East Of The Caspian Sea In Iran

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ABSTRACT

This study was designed to explore the status of the thyroid stimulating hormone [TSH] in the first trimester of pregnancy. In this analytical research, 'Project 120', apparently healthy pregnant women in their first trimester of pregnancy were selected randomly from pregnant women who visited the Danesh Medical Diagnostic Laboratory in Gorgan, which is located in northern Iran, during 2007-08. Serum TSH was measured by the Enzyme linked Immunosorbant Assay [ELISA]. The findings of this study indicated that 10% of pregnant women who also were apparently healthy subjects showed abnormal TSH serum concentration on the bases of the reference range of the laboratory kit used in this study, which seems to be incorrect. It is concluded here, that for the accurate measurement and the interpretation of thyroid hormones, the proper reference intervals in each region should be established to avoid confusion about the diagnosis of the thyroid function tests.

Key Words: Pregnant women, first trimester of pregnancy TSH, northern Iran.

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Introduction

Pregnancy is a physiological condition with varieties of new biochemical functions. Such a significant alteration happens in the maternal thyroid gland with a subsequent effect on the fetus. During the duration of pregnancy, the maternal thyroid function should be in proper condition to face the maternal and fetal physiological requirement during this period [20],[22],[25],[27] The subjects of thyroid function during pregnancy have been reviewed extensively by many researchers word- wide [6], [13], [24].

TSH is one the key hormones which regulates thyroid gland function. Some reports indicate the prevalence of TSH elevation and the significance of TSH measurement during pregnancy [1],[3],[4],[16],[29].There are various studies indicating the specific reference intervals of the thyroid hormone during pregnancy and arguing that the reference range of non -pregnant women should not be applied during pregnancy to assess the thyroid function tests [23],[28].

The proper evaluation of the thyroid gland is provided by the determination of other hormones which are produced and the antibodies which are raised against the gland. TSH is a single test which can draw

a clear picture of the thyroid function test and this hormone is regarded to be the most important hormone regulating the function of the thyroid gland [23]. This is also recommended by the American thyroid Association that has classified TSH, as the best single measurement of thyroid status due to the high sensitivity. [15]

Considering the cost- effectiveness of any laboratory test, it is advisable that the first line of any laboratory investigation for thyroid function determination can be started with the measurement of a single important test, which is TSH [13],[23]

The aim of this present study was to assess the status of serum TSH levels during pregnancy among apparently healthy pregnant women in Gorgan, in the north-east of Iran, which is located in the south-east of the Caspian Sea and to assess whether the serum TSH measurement with the manufacture's reference interval of non-pregnant can be a good and reliable starting point to check for any thyroid evaluations during the first trimester of pregnancy in this region or whether local reference intervals should be established to prevent the wrong diagnosis of thyroid function tests.

Materials And Methods

In this research project, 120 apparently healthy pregnant women who in their first trimester of pregnancy visited the Danesh Medical Diagnostic Laboratory in Gorgan, which is located in northern Iran, for the confirmation of pregnancy were selected during 2007-08. The exclusion criteria for pregnant women in this study was any history of thyroid disease and if the pregnant women had taken any medicines which were related to thyroid disease at the time of blood sampling. A questionnaire was filled up for each woman, which contained demographical characteristic, 2 ml of venous blood was taken from each pregnant woman and serum was obtained from each blood sample. Serum thyroid stimulation hormone [TSH] levels were determined by the Enzyme linked Immunosorbant Assay [ELISA], technique [6]

The reference intervals of the standard kit for the ELISA method in this study for TSH was [0.32- 5.2 MIU/L].

The findings of this study were entered into the computer. The SPSS-11.5 software and the Student's t test were used to analyze the data.

Results

In this present study, the pregnant women were in their first trimester of pregnancy, the mean of their maternal and gestational ages being 26.06 years and 7.79 weeks, respectively. The median of their maternal and gestational ages were 25 years and 4 weeks, respectively.

The mean serum TSH for our sample population in this study was 1.31mIU/L. The lower and upper values for serum TSH in this study were 0.1 and6.2 mIU/L in [Table/Fig 1]. The findings indicated that 10% of pregnant women had suppressed TSH levels and could be diagnosed .

Maternal serum TSH is presented for hyperthyroidism, which in our opinion can not be correct. In our earlier work we faced with the same problem, and we found that the same sample population demonstrated to have about 48% reduced thyroxine concentration [9] and therefore should have been evalutated further for hypothyroidism.We argued on that study although that those findings from laboratory point of view might be correct ,but clinically should not be taken seriously, because half of o apparently healthy pregnant women can not be labeled as hypothyroidism,. with findings in this present study ,we argue also that there is something wrong somewhere and it seems that the manufactrurer refrence interval kit for non-pregnant women can not be a base for evalution of pregnant women.This confusion raised also echoed by many others working in this area of research [14],[23] Considering our earlier work[9] with the present findings indicat

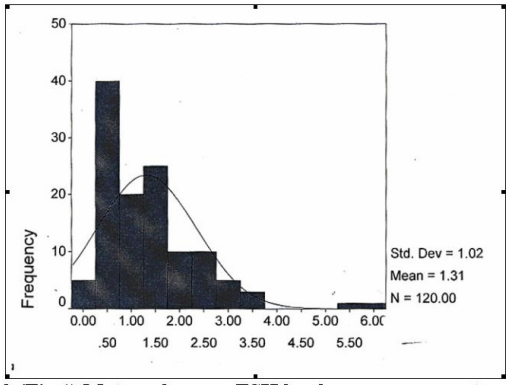
that there was not an acceptable correlation between the serum level of TSH and thyroxin serum concentration , which could be a base for misinterpretation of the thyroid function tests , with eventual harm to the fetus and the outcome of pregnancy. This problem in interpretation of thyroid function test during the first trimester of pregnancy was also reported by others[kurioka et al 2005]

In this present study according to our laboratory manufacturer's reference range, 10% of our pregnant women should be considered as hyperthyroidism cases and should be treated for thyroid hyperactivity. If the above findings was the base for drug prescription, the pregnant women would approach hypothyroidism with all its adverse effects on fetus [kurioka et al 2005].

In addition the pregnancy in women characterized by increasing demand of thyroxine. In addition, other studies indicated that during pregnancy even pregnant women with thyroxine therapy should be checked up further for an extra dose of required thyroxin in the early stage of pregnancy to prevent the possibility of neurophysiological damage to the growing foetus [24].

Our findings are in favor of establishing specific first- trimester reference intervals. Due the complex picture, the TSH and T4 concentrations have to be correlated and evaluated to prevent the risks involved with possible neurophysiologic and euro psychological events in our region. It should be noted that in pregnancy, non pregnant women reference intervals should not be the basis for the evaluation pregnant women. Our findings are in agreement with the results of other workers in various parts of the world.

Examples are China [10], Australia [23] India [28] Czech [13].



(Table/Fig 1) Maternal serum TSH level among pregnant women during first trimester of pregnancy.

Discussion

Serum TSH is considered to be the most important hormone whose levels can be used to assess thyroid function test during pregnancy and also, it can be extended to evaluate the thyroid status at any particular physiological condition. [3],[15], [23].

The clinical picture of thyroid function is better understood when all the key players of thyroid function tests such as thyroxin, [T4] triidothyronine [T3], T3 uptake, antibodies produced against peroxides and thyroglobulin [Anti TPO, Anti Tg] are measured, [7] but due to the high expenses involved in measuring these factors, it is considered best to recommend the most important test which gives the clue for thyroid function, which is TSH. It has also been recommended by others [17],[23] In our study, we measured TSH levels of apparently pregnant women in order to have a thyroid hormone test during a normal routine pregnancy, which is most important for the gynecologist and the pregnant women themselves for the outcome of their pregnancy. The adverse complications related to thyroid dysfunction in pregnant women [22], the clear status of the thyroid function of pregnant women and the correction of abnormalities is of utmost importance and have been the topics of many researches, but there has been no comprehensive argument on whether to screen the pregnant women for their thyroid hormone status [8]. In spite of substantial reports word- wide on the risks

involved if the hypothyroidism in particular, was not diagnosed in the early stage of pregnancy [22],[27], there are rare reports that maternal thyroid dysfunction does not always play an adverse effect on the pregnancy outcome [21] Comprehensive literature review does not end up with the above finding and there are universal agreements on the need of thyroxin substitution when maternal thyroxin levels are not enough for the outcome of pregnancy and the growing foetus. [13], [20],[25]

Although there are reports encouraging the assessment of the thyroid function test with ultimate correction of any dysfunction [14], the reference intervals and the methodology of thyroid hormone determination is of utmost importance [5],[11],[13] in addition to the environmental factors, ethnicity and the nutritional habits in one region, which should be taken into account for any interpretation of results for the thyroid status in pregnant women [16], [30].

Our findings in this research project indicated that according to the method and laboratory kits that we used and the given reference interval of our method [0.32-5.2 mIU/l], 10% of pregnant women in this region have the serum TSH levels below lower limit of normal values <0.32 mIU/L]. The mean serum TSH was 1.3mIU/L, which was far away from the higher limit of the normal range in this study which was 5.2mIU/L.

Our earlier reports on the serum T4 levels among the same pregnant women also showed that 48% of pregnant women had T4 concentrations >12.5 microgram/ dl [9]. The reference interval of our method for T4 was [4.7-12.5 microgram/dl] and therefore, according to our findings and due to the manufacturer's reference range that we used, 48% and 10% of our pregnant women remained in the hyperthyroid status according to the serum T4 and TSH levels, which logically cannot be true, because the pregnant women whom we randomly selected were apparently healthy without any thyroid dysfunction. On the other hand, if we had 48% of pregnant women with elevated T4 [9], logically we should have had far more suppressed TSH levels. On the basis of our findings in this study and our earlier reports, we argue that the manufacturer's reference interval that we used for the interpretation of results of the thyroid function test is not fully correct and the way that these women's thyroid function tests were evaluated, can lead to misdiagnosis. We assume that a considerable misclassification of thyroid function tests occurred when the manufacturer's normal range of TSH [0.32- 5.2 mIU/L] and T4 [4.7- 12.5 microgram/dl] was considered as the guideline to interpret the findings of the thyroid function tests.

It this present study, our data clearly predicted that some miscalculation occurred when the above mentioned reference intervals were used to approach pregnant women and if the thyroid function tests in this study was considered an important tool for the evaluation of pregnancy there would a definite misdiagnosed directed by the laboratory results. It should be emphasized that the specific reference intervals for non-pregnant women cannot be applied to interpret the thyroid function tests of pregnant women, a practice which gives clinicians the incorrect advice to approach the thyroid status in pregnant women [10]. Our findings were confirmed by other studies which argued that a miscalculation occurred when thyroid function tests results were interpretated in pregnant women and they were compared using non- pregnant reference range intervals [2],[12],[13],[14],[28]

Stricker et al in their study reported that 10.4% of the potential misclassifications of thyroid function tests were found when the non- pregnant women normal range was used for pregnant women. In another study, while screening for thyroid function during pregnancy, the reference interval for TSH was considered to be [0.27- 4.2 mIU/l]. If this normal range was to be considered for our pregnant women, we would have had fewer pregnant women with suppressed TSH. The interpretation

of our findings on the basis of this latter reference interval was different and less than 10% of our pregnant women who were considered to be hyperthyroid now have a normal thyroid status.

In a separate study, the reference interval for TSH was established to be [0.06-3.67mIU/L] on the basis of this latter normal range. Also, for none of our pregnant women who were considered to have thyroid dysfunction, was our normal range for TSH 0.32-5.2 mIU/L [3] .

There are various reports suggesting trimester- specific reference intervals for thyroid function. Particular attention was applied to the first- trimester specific range due the critical phase of early pregnancy during which the brain develops within the fetus

Above all, trimester specific intervals in each particular region also should have been taken into consideration when thyroid function tests in pregnant women were evaluated [4], [17]

Conclusion

Finally, on the basis of the findings from this study, we conclude that in this region within northern Iran:

•] The establishment of the reference interval for TSH levels during the early stage of pregnancy is of utmost importance if the thyroid function test is to be evaluated properly.

•] The reference interval of non-pregnant women cannot be applied for pregnant women due to a potential misclassification which might have occurred when thyroid function tests were assessed.

•] Our pregnant women were apparently healthy subjects. We conclude that the reason why we had 10% of pregnant women with suppressed TSH levels is due to the above miscalculation and misclassifications of the reference range.

•] Further studies should have been done to establish the pregnant women reference interval in this region of Iran to avoid the misinterpretation of thyroid function tests during pregnancy, which might have irreversible consequences for the growing fetus.

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