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ORIGINAL ARTICLE

Deiodinase 1 serum levels in the second trimester of pregnancy

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SUMMARY

Thyroid disease is one of the most frequent causes of gestational endocrinopathies. Deiodinases play an important role controlling the concentration of thyroid hormones at the tissue level and the homeostasis of thyroid hormones, on pregnant women; specifically, Deiodinase type 1 (D1) may control the TSH levels.

To determine the serum levels of D1 in Mexican pregnant women who are in the second trimester of pregnancy.

A prospective, descriptive, and cross-sectional study was carried out with a sample of 52 patients in their second trimester of pregnancy who attended the outpatient clinic of the "Mónica Pretelini Sáenz" Maternal Perinatal Hospital (HMPMPS), in Toluca, Mexico. A peripheral blood sample was taken to quantify the values of D1 and TSH. The Spearman rank correlation coefficient test using SPSS statistics version 21 software was tested between these two variables.

D1 mean value was of 491.3 pg / mL (± 340.48), TSH mean value was 5.25 mIU / mL (± 3.34), and rs = 0.023 (p = 0.869) was found.

Discussion: Based on the study result, the use of D1 quantification to observe

changes in maternal TSH has a non-significant weak positive correlation, restricting its usefulness for timely diagnosis of thyroid abnormalities during pregnancy.

The use of D1 quantification during the second trimester of pregnancy did not show significance to determine thyroid alterations in relation to TSH values in the Mexican population.

Introduction

Thyroid disease is the second cause of gestational endocrinopathies with a prevalence of 4%, only after gestational diabetes. Thyroid disease carries an adverse maternal and fetal outcome, even in the mildest forms it also triggers maternal-fetal complications such as preterm delivery, pre-eclampsia, gestational loss, and low birth weight (Fernández Vaglio, 2020; Steegborn, 2020).

Deiodinases are selenocysteine-dependent membrane-bound proteins (SelCys) that play a fundamental role in the homeostasis of thyroid hormones (TH) by participating in the activity of the hypothalamic-pituitary-thyroid axis and by controlling the concentration of thyroid hormones at the tissue level (Morris, 2019; Luongo, 2019).

Changes in thyroid hormone levels and ratios have been suggested to be associated with genetic variation in genes encoding the enzyme deiodinase (Bianco, 2018). It has also been observed that a transitory decrease in its enzymatic activity can manifest itself in fasting or in an acute illness (Llop, 2017; França, 2021). Thyroid disease carries an adverse maternal and fetal outcome, even in the mildest forms (Gargallo Fernández, 2013; Korevaar, 2017; Lucas Javato, 2018; Donnay Candil, 2021).

In the general population, thyroid function tests are sufficient to detect this endocrinopathy, but during pregnancy the established values of these tests change, commonly leading to misdiagnosis of euthyroidism and undiagnosed cases of subclinical hypothyroidism during pregnancy (Koulouri, 2013; Joosen, 2016). The objective of this study was to determine the serum levels of deiodinase 1 in Mexican pregnant women who are in the second trimester of pregnancy.

Material and methods

A prospective, descriptive, and cross-sectional study was carried out with a sample of 52 patients in their second trimester of pregnancy who attended the outpatient clinic of the "Mónica Pretelini Sáenz" Maternal Perinatal Hospital (HMPMPS), Health Institute of the State of Mexico (ISEM), in Toluca, Mexico.

The inclusion criteria were pregnant women between the 14th and 27th week of gestation, of reproductive age and cared for in the HMPMPS.

Exclusion criteria were patients with thyroid endocrinopathy; recent surgery; malignancy; without informed consent/assent; medical indication for consumption of levothyroxine, methimazole, propylthiouracil, twin pregnancy or miscarriage.

The elimination criteria were not having D1 and / or TSH quantification, an insufficient sample for the study, or a poorly taken sample.

Weight and height were measured to one decimal place while wearing the patient light clothing and without shoes, using a calibrated digital scale with stadiometer (Seca). Body Mass Index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2).

After consent / informed assent, a peripheral blood sample was taken to quantify D1 and TSH were measured by ELISA on an ELx800 ™ device (BioTek Instruments, Inc.) at the Research Laboratory of Ciprés Grupo Médico S.C. (CGM).

Through the Microsoft Excel data analysis program, the variables were analyzed descriptively with measures of central tendency. To assess the association between quantitative variables, the Spearman's rank correlation coefficient was used through the SPSS statistics version 21 software. The p value was considered significant at < 0.05.

This project was approved by the Ethics and Research Committee of the HMPMPS (code: 2021-06-741). No risk was attributed to pregnant women or their neonates according to the regulations of the General Law on Health in Research Matters, and it was adhered to the Declaration of Helsinki (Fortaleza, Brazil).

Results

52 patients who attended the hospital outpatient clinic were studied (Table 1), on average they had an age of 24.98 ± 7.5 years, the women were in the 20.47 ± 3.26 WG as a mean and between their first and fourth pregnancy, with an average of 1.88. They also had a BMI of 26.75 ± 4.99 on average and a weight gain during pregnancy of 1.75 ± 4.17 kg.

When calculating the D1 values, the mean was 491.31 ± 340.48 pg/mL, while the TSH values had a mean of 5.25 ± 3.34 mIU/mL. When analysing with the Spearman correlation, an rs = 0.023 (p = 0.869) was found.

Table 1: Results of pregnant women

	Mean	Standard deviation
Age (years)	24.98	7.51
Gestational period (weeks)	20.47	3.26
Gestation (number)	1.88	1.08
Deliveries (number)	1.46	0.66
Cesarean sections (number)	1.13	0.35
Miscarriages (number)	1.36	0.67
Weight gain (kg)	1.75	4.17
Body Mass Index (kg/m^2)	26.75	4.99
TSH (mIU/mL)	5.25	3.34
D1 (pg/mL)	491.31	340.48

D1: deiodinase 1, TSH: Thyroid stimulating hormone.

Discussion

The mean value of TSH in the 52 pregnant patients in their second trimester of pregnancy in the present study was 5.25 ±3.34 mIU/mL, in disagreement with the TSH values reported by Joosen et al. of 3.39 mIU/L and 3.38 mIU/L in the first and second trimesters, respectively, in pregnant women of Caucasian origin (Joosen, 2016).

According to the Mexican medical practice guideline, the mean TSH value in our population is too low to consider the presence of clinical hypothyroidism (TSH greater than 10 mIU/L regardless of FT4 concentrations) but does not rule out the presence of a subclinical hypothyroidism, having a TSH level greater than 2.5 mIU/L. The results obtained support the notion that interpretation of thyroid function tests in pregnant women is challenging and requires more specialized complementary studies, in

addition to the greater weight of clinical diagnosis (Koulouri, 2013; Joosen, 2016; CENETEC, 2016).

On the other hand, the mean value of D1 491.31 ± 340.48 pg/mL could not be compared with other studies carried out in pregnant women due to the lack of literary resources in this area. However, the important activity of this enzyme in controlling systemic levels of thyroid hormones and maintaining the euthyroid state by facilitating the rapid release of self-generated T3 back into the circulation is highlighted.

An adequate concentration of TH is essential for the normal development of the fetus during pregnancy. In the early stages of pregnancy, especially during the first trimester, the mother provides TH, so the concentration of oxygen in the fetus depends directly on transport and regulation through the placenta to be released into the fetal blood. Even after the start of fetal thyroid hormone secretion, the maternal contribution represents 30 to 60% of fetal T4, necessary for adequate neurodevelopment (Ruiz Ochoa, 2016; Gutierrez-Vega, 2020; Falla-Zúñiga, 2021; França, 2021).

TH, in addition to influencing fetal tissues, are involved in the proliferation, survival, differentiation and invasiveness of the trophoblast in the placenta. In the trophoblastic cell membrane, enzymes D2 and D3 modify the biological activity of HT. This suggests that the activity of D2 is a homeostatic mechanism of T3 at the placental level. Instead, D3 plays an important role in maintaining low levels of T3 in the fetus, thus preventing catabolic excess. Therefore, deiodinases are responsible for the fine regulation of T3 and T4, which will ultimately be transported to the fetus (Ruiz Ochoa, 2016; Gutierrez-Vega, 2020; Falla-Zúñiga, 2021; França, 2021).

As pregnancy progresses and until the end of gestation, the expression of deiodinases gradually decreases in relation to the downward transfer of TH from the mother to the fetus (Ruiz Ochoa, 2016; Falla-Zúñiga, 2021).

Among all the endocrinopathies that occur during pregnancy, thyroid disorders are one of the most frequent and lead to potentially fatal complications in the maternal-fetal binomial (Ayala-Yáñez, 2016), hence the importance of a timely diagnosis using other tools not contemplated in the routine thyroid profile, whose interpretation is limited by changes in the hypothalamus-pituitary-thyroid axis that develop during pregnancy.

Thus, to our knowledge, this is the first study that quantifies serum D1 levels in pregnant women during their second trimester. Based on the study result, the use of D1 quantification to observe changes in maternal TSH has a non-significant weak positive correlation, restricting its usefulness for timely diagnosis of thyroid abnormalities during pregnancy.

The main limitations of the study were the heterogeneity in the population, the lack of knowledge of the maternal thyroid status prior to pregnancy. The creation of new protocols with the use of D1 quantification in pregnant women using a larger population or the development of other investigations with new tools that allow early identification of thyroid abnormalities during pregnancy is suggested.

Conclusion

The use of D1 quantification during the second trimester of pregnancy did not show significance to determine thyroid alterations in relation to TSH values in the Mexican population. Denoting the need to develop new tools that allow early guidance on the existence of life-threatening thyroid disorders during pregnancy.

Conflicts of Interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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