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RESEARCH ARTICLE

Immunohistochemical Study of Placentas of Pregnant Women with Hypothyroidism Compared to Healthy Individuals in Zahedan City

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ABSTRACT

Background: Thyroid hormones are crucial for fetal health and placental development. **Aim:** To investigate immunohistochemical changes in placentas of pregnant women with hypothyroidism compared to healthy individuals. **Materials and Methods:** A total of 200 placentas (100 hypothyroid and 100 healthy) were analyzed for histopathological parameters including syncytial nodes, hyalinization, calcification, and cytotrophoblastic proliferation. **Results:** All studied parameters were significantly higher in the hypothyroid group compared to controls. **Conclusion:** Hypothyroidism during pregnancy significantly affects placental morphology, emphasizing the need for early diagnosis and treatment.

Keywords: Hypothyroidism, immunohistochemistry, placenta

INTRODUCTION

Thyroid hormones are among the hormones responsible for a wide range of metabolic functions, growth and development, and caloric and heat production in the body. Changes in thyroid hormones during pregnancy have many effects on the placenta and fetus.[1] A deficiency in thyroid hormone production is considered hypothyroidism, which can manifest in abnormal pregnancies.[2] The complications of hypothyroidism in pregnant women, if not prevented and treated, include premature birth, miscarriage, birth complications, fetal abnormalities, pre-eclampsia, low birth weight, and fetal death. Serum levels of thyroid hormones decrease in the second half of pregnancy, which can be a challenging issue.[3] The decrease in thyroid hormones during this period is influenced by various factors that can be responsible for the moderate to severe decrease in thyroid hormone levels during pregnancy.[4] In fact, in hypothyroidism in pregnant women, the thyroid-stimulating hormone (TSH) concentration level is high, and the thyroxine hormone (T4) level in the blood serum is normal, which is called subclinical hypothyroidism.[5] Hypothyroidism in pregnant women poses complications, including an increased risk of the fetus developing the condition.[6] It can also lead to issues, such as placenta previa, retroplacental hematoma, arterial desceval, and inflammatory lesions. Thyroid hormones play a crucial role in the development of the fetal nervous system, so untreated hypothyroidism may result in neurological disorders.[7] In addition, untreated hypothyroidism can negatively impact the intelligence of the child. The placenta, which serves as a specialized organ between the mother and the developing fetus, can be affected by histological changes due to complications, such as high blood pressure, diabetes mellitus, and hypothyroidism, ultimately impacting fetal health.[8] This study aimed to investigate the immunohistochemical changes in the placenta of pregnant women with hypothyroidism compared to those of healthy pregnant women.

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MATERIALS AND METHODS

Group Design

In this study, pairs of pregnant women who were referred to the Obstetrics and Gynecology Clinic of Imam Ali Hospital in Zahedan city were used. One hundred pairs of pregnant women with hypothyroidism and one hundred pairs of pregnant women without hypothyroidism were collected and included in the study. The group of pregnant women with hypothyroidism was selected based on the diagnosis of obstetricians and gynecologists, clinical tests, and measurements of TSH serum concentration, as well as T3 and T4 values. The studied pregnant women were 20–35 years old. An informed consent form was obtained from these patients so that their health status could be examined in terms of risk factors, such as congenital or acquired heart diseases, obesity, multiple pregnancies, diabetes, high blood pressure, and smoking.

Inclusion Criteria

- Fresh placenta
- Pregnant women with hypothyroidism
- Pregnant women with a history of pre-mature birth
- In the control group, pregnant women were examined who did not have any disease and their biochemical tests were normal.

Exclusion Criteria

- Pregnant women who had another disease during pregnancy other than hypothyroidism
- Damaged placenta
- Women who were not willing to cooperate in the study
- Pregnant women who were not willing to cooperate in sample collection.

Immunohistological Examination

To conduct the immunohistochemical test, placentas from the studied women were collected in the delivery room immediately after birth and washed with running water. Sections of the placenta, including both the basal and fetal planes, were obtained and preserved in 10% formalin. Following tissue processing, 5 μm sections were sliced using a rotary microtome, stained with hematoxylin and eosin, and examined under a light microscope. The collected data were entered into Microsoft Excel for analysis, with a $P < 0.05$ considered statistically significant when comparing the case and control groups.

RESULTS

In this study, 100 pregnant women with hypothyroidism were considered cases and 100 healthy pregnant women as controls. Clinical characteristics of the pregnant women studied, such as placental weight, maternal age, and gestational age, are shown in Table 1, and the study found that there was no statistically significant difference between the two groups. Microscopic examination of the placenta showed the presence of syncytial nodes, hyalinized villi, calcification, and cytotrophoblastic proliferation of fetal vessels. Peripheral and central sections of the placenta were examined regarding microscopic parameters in the low-power field. The results showed that the number of all microscopic parameters in the group with hypothyroidism increased compared to the control group, and there was a statistically significant difference between the two studied groups [Table 2]. In addition, the results of the research showed that the pathological changes in the placenta of pregnant women with hypothyroidism and the data indicated a significant difference.

DISCUSSION

The placenta requires several hormones from the mother to function effectively in nourishing and supporting the growth of the fetus.[9] One essential

Table 1: Statistical analysis of clinical characteristic

Characteristics	Control group (n=100)	Hypothyroid group (n=100)	Statistical significance (P<0.05)
Mean placental weight	460.2±64.3	466.5±115.2	Not significant
Mean maternal age	20.5±2.6	21.6±4.0	Not significant
Mean gestational age/day	350.7±12.5	360.5±14.3	Not significant

Table 2: Comparative immunohistochemical results of the study

Characteristics	Control group (*n*=100)	Thyroid group (*n*=100)	*t*-test	*P*-value	Significance
Syncytial knot	6.03±2.61	10.58±4.5	−5.215	0.00000	Highly significant
Hyalinization	3.15±1.19	10.12±7.02	−8.428	0.00000	Highly significant
Calcification	2.20±1.33	5.44±3.07	−14.351	0.00000	Highly significant
proliferation of the inner lining of fetal blood vessels	4.55±1.33	3.88±2.32	6.234	0.00000	Highly significant
Cytotrophoblastic proliferation	7.53±2.43	7.76±4.16	−0.778	0.36467	Not significant

hormone is thyroid hormone. Research indicates that fluctuations in thyroid hormone levels can impact placental function, which in turn affects the growth and nutrition of the fetus. Hypothyroidism in pregnant women can lead to adverse effects on both the placenta and the developing fetus.[10] Our study found no statistically significant differences in placental weight, maternal age, or gestational age between the two groups, pregnant women with hypothyroidism and healthy pregnant women. However, we did observe statistically significant differences in the immunohistochemical changes of placental villi, including proliferation of the inner lining of fetal blood vessels, syncytial knot, calcification, and hyalinized areas between the case and control groups. An immunohistochemical study conducted by Kemkem *et al*. found that pregnant women with hypothyroidism had a significant increase in the number of syncytial nodules, stromal fibrosis, and hyalinization compared to healthy pregnant women.[11] These findings align with the results of our study. The results of the study by Andersen *et al*. showed that syncytial nodes are usually observed in placentas with accelerated villous maturation because syncytial nodes are a reflection of placental maturation.[12] The results of our study also show that delayed villous maturation occurs in the placentas of pregnant women with hypothyroidism. The results of the study by Campbell *et al*. showed that calcification was higher among healthy pregnant women without hypothyroidism, which is inconsistent with the results of our study.[13] One reason for this could be the increased incidence of post-term pregnancies among the control group. The results of the study by Eshkoli *et al*. showed that there was no statistically significant difference between the immunohistochemical factors studied in the placenta of pregnant women with hypothyroidism, such as syncytial nodules and chorangiosis, which was in line with the results of our study.[14] In another immunohistochemical study conducted by Muller *et al*. on the surface area and diameter of villi in the placentas of pregnant women with hypothyroidism, it was shown that the surface area and diameter of villi were lower in placentas with hypothyroidism, and there was a statistically significant difference between the two groups of cases and controls.[15] Furthermore, in line with the studies of Ribeiro *et al*. it was shown that stillbirth in the group of pregnant women with hypothyroidism is significantly increased compared to healthy pregnant women due to maternal and fetal vascular lesions, including retroplacental hematoma, parenchymal infarction, fibrin deposition, fetal vascular thrombosis, and avascular villi.[16] In addition, parenchymal infarctions in pre-mature stillbirths were more common in these women than in healthy pregnant women. Another study conducted by Ge *et al*. showed increased syncytial node formation in the placenta of pregnant women with high blood pressure, which indicates that factors, such as increased blood pressure are as effective as hypothyroidism in causing placental and fetal lesions.[17]

CONCLUSION

The results of our research showed that the hypothyroidism of the mother has a negative effect on factors, such as all microscopic parameters, which subsequently has a negative effect on the growth of the fetus and the placenta. According to immunohistochemical studies, these factors have beneficial effects in the early diagnosis and treatment of pregnant mothers suffering from hypothyroidism, reducing fetal and placental developmental abnormalities and complications, such as mortality.

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AUTHORS' CONTRIBUTION

The authors contributed to the research conception and design. All authors studied this draft and contributed to and confirmed the final manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest regarding the publication of this paper.

DATA AVAILABILITY

The dataset presented in the study is available on request from the corresponding author during submission or after publication.

ETHICAL APPROVAL

The study has a code of ethics (IR.IAU.ZAH.REC.1400.042).

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The study was approved as a research project in the Faculty of Medicine of the Azad University of Zahedan.

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