


## The Effects of Hypothyroidism on Maternal Health

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### ABSTRACT

**Background & Objective:** Hypothyroidism leads to an increased risk of overweight and obesity. This study examined the effect of weight gain caused by hypothyroidism on maternal health (hypertension, gestational diabetes, and miscarriage) for the first time.

**Materials & Methods:** This case-control study consisted of 123 pregnant women with clinical hypothyroidism and 242 non-hypothyroid pregnant women as the control group. National guidelines were used to diagnose hypothyroidism in the first trimester. Body mass index (BMI), thyroid-stimulating hormone level, as well as systolic and diastolic blood pressure (BP) were measured. Moreover, fasting blood sugar was assessed during 24-28 weeks of gestation. Data were analyzed by the Chi-square, Student's t-distribution, and logistic regression using the SPSS19 software.

**Results:** We found a significant relationship between BMI and hypothyroidism in pregnant women ( $P < 0.001$ ). Systolic and diastolic BP in the case group were higher in women with  $BMI \geq 25$  ( $P = 0.017$  and  $P = 0.002$ ). Furthermore, diastolic BP had a significant impact on abortion ( $P = 0.018$ ). The rate of abortion increases by 1.042 with 1 mmHg elevation in diastolic BP in pregnant women if the variables maternal age, hypothyroidism, and overweight are constant.

**Conclusion:** According to the results of the present study, weight gain in women with hypothyroidism can affect the risk of high diastolic BP and abortion.

**Keywords:** Abortion, Hypertension, Hypothyroidism, Obesity, Overweight



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### Introduction

The prevalence of hypothyroidism has been reported to be 2.5%-7.5% in several studies (1). Since most thyroid disorders are autoimmune, the incidence rate in women is 10 times higher than in men (2). Thyroid disorders are common in young females and pregnancy affects the physiology and function of the thyroid in mothers (3). Thyroid function in pregnancy may change due to different causes, such as iodine deficiency, human chorionic gonadotropin (hCG), and estrogen (4). The thyroid gland in a fetus is not active before the 20<sup>th</sup> week of pregnancy. Therefore, the brain in a fetus is specifically dependent on the mother in terms of thyroid hormones.

Any type of hypothyroidism (i.e., primary and subclinical) with any causes increases the risk of abortion, preeclampsia, low birth weight, and premature birth along with reducing the intelligence quotient (IQ) of a child (5). Thyroid disorders cause mother and fetus injuries. Women with thyroid disorders experience abnormal

hemorrhage, recurrent miscarriage, ovarian failure, gestational diabetes mellitus (GDM), preterm labor, admission at NICU, and neonatal death (6).

Hypothyroidism in a pregnant mother results in intrauterine growth retardation, developmental neuropsychiatric disorders of the fetus, low birth weight, respiratory distress syndrome, spontaneous abortion, fetal death, infertility prevalence, premature birth, placental abruption, and preeclampsia. Moreover, subclinical hypothyroidism is a risk factor for abortion before the 20<sup>th</sup> week of pregnancy (7). Subclinical hypothyroidism is usually associated with adverse outcomes. Untreated subclinical hypothyroidism in pregnant women is associated with higher risk of placental abruption, pregnancy loss, neonatal death and premature rupture of membranes (8).

A high body mass index (BMI) may be one of the signs of hypothyroidism. Obesity is a common problem in

pregnancy that affects mother and fetus causing short- and long-term complications for mothers, such as increasing the risk of GDM and preeclampsia (9). In addition, the risk of spontaneous abortion is 1.67 times higher among overweight and obese women (10). Some studies found that the placentas of obese women have higher lipid content (11).

Pre-pregnancy overweight can augment cesarean delivery and the rate of preeclampsia increases by 0.1% in these women (12). Several investigations demonstrated that the rate of low birth weight and preeclampsia are higher in obese adolescent women (13, 14). Obesity is considered a risk factor for gestational hypertension (15).

Hypertension is uncommon during pregnancy and the lack of treatment for hypertension is a risk factor for both mother and child. High BMI during pregnancy has an incremental influence on systolic and diastolic blood pressure (BP) (16). Recent studies have shown an increase in diastolic BP in women with preeclampsia (17, 18). For every 10 mm Hg diastolic BP increase, the risk of abortion is 18% higher (19).

Considering the prevalence of obesity and the fact that obesity affects both mother and child health, this study investigated the effect of weight gain resulting from gestational hypothyroidism on maternal health complications, including hypertension, GDM, and abortion.

## Materials and Methods

### Subjects

In order to monitor hypothyroidism during pregnancy, all pregnant women refer to the gynecology clinic in the first trimester of pregnancy and are included in the national hypothyroidism monitoring plan during the first trimester. According to our national guidelines, the normal range of thyroid-stimulating hormone (TSH) levels is 0.2-3.99  $\mu\text{U/mL}$  in the first pregnancy trimester.

A total of 365 pregnant women were included in this case-control study, of which 123 individuals with the symptoms of hypothyroidism were considered as the case group and 242 healthy pregnant women were considered as the control group. The participants in the two groups were similar in terms of maternal and gestational age. All the patients were outpatients at the Obstetrics Clinic of Imam Hossein Hospital, Bijar affiliated to the Kurdistan University of medical sciences, Iran in 2017.

Approval was obtained from the Ethics Committee of Hamadan University of Medical Sciences, Iran with the code of IR.UMSHA.REC.1397.265.

### Measurements

#### BP and BMI

The BP of participants was measured at a sitting position by Welch Allyn digital blood pressure device. Bodyweight was measured with an accuracy of 0.1 kg applying a balanced-beam scale. Height was measured

with a stadiometer with an accuracy of 0.5 cm. The BMI of individuals was calculated based on the  $\text{weight}/(\text{height})^2$  formula.

#### TSH

Blood samples were collected at 8-9 a.m. after at least 12 h fasting. The TSH level was examined by enzyme-linked fluorescent assay (ELFA) using the VIDAS instrument. The detection limit of the ELFA method is 0.05  $\mu\text{U/mL}$  for TSH.

#### Proteinuria

According to the American College of Obstetricians and Gynecologists (ACOG) guideline, preeclampsia is proteinuria of 300 mg and/or +1 on urine test strips after 20 weeks of pregnancy in combination with systolic blood pressure (SBP) $\geq$ 140 mmHg and a diastolic BP $\geq$ 90 mmHg.

#### Blood Glucose

Blood glucose level was measured during weeks 24-28 of gestation to monitor GDM. The blood glucose level was analyzed by an enzymatic method using a commercial kit (Pars Azmun, Iran) according to the instructions of the manufacturer.

#### Statistical Analysis

The results of descriptive statistics are presented as mean $\pm$ SD. Data were analyzed by the Chi-square, Student's t-distribution, and logistic regression using the SPSS software version 19 (IBM, Chicago, Ill., USA). The significance level was considered  $P\text{-value}<0.05$ .

## Results

The mean age of studied individuals was 30 years old with the youngest and oldest being 14 and 45 years old, respectively. The study groups were matched for maternal age ( $P=0.688$ ). Moreover, the groups were similar in terms of gestational age as all mothers were in the first trimester.

[Table 1](#) represents the mean of the examined parameters in the two groups calculated by the Mann-Whitney U test. According to the outputs of the Chi-square test, BMI and hypothyroidism were significantly related in pregnant women ( $P<0.001$ ). The prevalence of hypothyroidism in overweight women (BMI $\geq$ 25) was 3.046 times higher than the individuals in the control group.

Regardless of the grouping variable, there was no significant difference between the systolic and diastolic BPs of overweight participants (BMI $\geq$ 25) and individuals with normal weight (BMI $<$ 25). However, different results were observed for the mean BPs in both groups based on BMI ([Table 2](#)).

Furthermore, the mean abortion in both groups was evaluated based on BMI ([Table 3](#)). Separate univariate regression analyses showed that diastolic BP affected abortion significantly ( $P=0.018$ ), while SBP had no significant influence on abortion ( $P=0.069$ ). Neither

hypothyroid variables ( $P=0.530$ ) nor BMI ( $P=0.553$ ) significantly affected abortion.

Finally, multiple logistic regression was used to determine the simultaneous effects of maternal age, hypothyroidism, overweight, and BP on the abortion rate. According to the results of this analysis presented in [Table 4](#), only maternal age and diastolic BP influenced the rate of abortion. Hypothyroid and BMI variables were not related to abortion.

If some variables, namely maternal age, hypothyroidism, and overweight are constant, abortion increases by 1.042 for each 1 mmHg augmentation in the diastolic BP of a pregnant mother. Moreover, if some variables, including BP, hypothyroidism, and overweight are constant, the rate of abortion elevates by 1.06 for each unit of raise in the age of the pregnant mother. In other words, both the age and BP of a pregnant mother have a positive effect on the abortion rate.

**Table 1. Mean of the parameters studied in both groups.**

Variable	Control group (n=242)	Hypothyroidism group (n=123)	P-value
TSH <sup>a</sup>	2.2166±5.6813	4.2849±3.8964	<0.001
BMI <sup>b</sup>	24.6736±5.3769	27.1236±4.5655	<0.001
Age	30.3182±6.8063	30.0244±6.2047	0.688
Systolic BP <sup>c</sup>	103.1777±8.7285	106.0976±11.0427	0.011
Diastolic BP	64.9504±6.7870	66.6829±6.2716	0.019
Abortion	0.2149±0.4115	0.2439±0.431	0.531
FBS <sup>d</sup>	86.9835±10.5112	89.0569±9.0193	0.063

a, thyroid stimulating hormone; b, body mass index; c, blood pressure; d, fasting blood sugar

**Table 2. Mean systolic and diastolic blood pressure in both groups according to BMI.**

Variable		BMI≥25 (Mean±SD)	BMI<25 (Mean±SD)	P-value
Systolic BP <sup>a</sup>	Hypothyroidism	110.000±11.792	104.667±10.461	0.017
	Control	102.346±7.584	103.278±8.867	0.608
Diastolic BP	Hypothyroidism	69.576±6.175	65.622±5.997	0.002
	Control	66.615±6.682	64.759±6.793	0.189

a: blood pressure

**Table 3. Mean abortion in both groups according to BMI.**

Variable		BMI≥25 (Mean±SD)	BMI<25 (Mean±SD)	P-value
Abortion	Hypothyroidism	0.259±0.441	0.217±0.417	0.600
	Control	0.239±0.428	0.200±0.401	0.474

**Table 4. Logistic regression analyses of diastolic BP and other confounding variables to predict abortion.**

Dependent variable	independent variable	B±S.E	Wald statistic	OR	P-value
Abortion	Diastolic BP <sup>a</sup>	0.041±0.020	4.307	1.042	0.038
	Age	0.058±0.020	7.996	1.060	0.005
	Group	0.113±0.281	0.162	1.120	0.688
	BMI <sup>b</sup>	0.004±0.032	0.017	1.004	0.898

a, blood pressure; b, body mass index

## Discussion

Thyroid disease is the second most common endocrine disorder after diabetes in women of reproductive age. There are similarities between the symptoms of thyroid disease and pregnancy. Therefore, problematic disease diagnosis causes a delay in a definitive diagnosis, which can be followed by irrecoverable effects for both mother and fetus (19).

The high prevalence of overweight and obesity following hypothyroidism, specifically during pregnancy, can cause problems. Obesity can lead to BP disorders and preeclampsia. The findings of the present study differed from the results reported by previous studies. However, our results indicated that weight gain in women with hypothyroidism can influence the increase in diastolic BP and abortion.

Lotfalizade *et al.* observed subclinical hypothyroidism in 212 out of 1,000 pregnant women in the first trimester in Mashhad, Iran. The researchers divided pregnant women with subclinical hypothyroidism into two treated and untreated groups. Their results indicated that the rates of placental abruption and premature birth were significantly higher in the untreated group. However, the two groups had no significant difference in terms of preeclampsia prevalence. It is believed that SBP  $\geq 140$  mmHg and diastolic BP  $\geq 90$  mmHg are the signs of preeclampsia. Consequently, the present study did not consider the hypothyroid factor.

The results showed that the rate of abortion augmented by 1.042 for each 1 mmHg increase in diastolic BP. Moreover, abortion was elevated by 1.06 for each unit of raise in the age of mothers. Furthermore, we found a significant relationship between BMI and hypothyroidism in pregnant women (20).

Our study revealed a significant relationship between hypothyroidism and BMI in women as hypothyroidism had an occurrence of 3.046 times higher in obese participants than the normal weight ones. These results were consistent with the findings of Cheng *et al.* in China. They found TSH to be significantly related to FT4 levels and weight gain in obese pregnant women (13). Mosso *et al.* demonstrated that higher BMI in the first trimester was accompanied by decreased thyroid function in women in Chile. According to the results of the present study and the mentioned researches, high BMI may be a sign of hypothyroidism (19).

Another study by Pop *et al.* showed no relationship between hypothyroidism and BMI in the 12<sup>th</sup> week of pregnancy. Their findings were not in line with our results because we examined pregnant women in the first trimester. In the current study, the age range was higher than the study conducted by Pop (21). Yang *et al.* indicated that subclinical hypothyroidism enhanced recurrent miscarriage in China. Although the present study did not find a direct effect for hypothyroidism on abortion, significant relationships were observed between hypothyroidism and BMI, as well as diastolic

and systolic BPs. Therefore, hypothyroidism is expected to indirectly affect abortion (22).

Previous studies have proven that high serum TSH level is correlated with spontaneous abortion, hypertensive disorders, and preterm birth. In the present study, in line with previous studies, hypothyroidism increased BP and possibly the risk of miscarriage during pregnancy (23, 24).

Moreover, high levels of TSH were reported in obese non-pregnant women. Diverse mechanisms are involved in the impact of obesity on TSH augmentation by activating endocrine organs. In addition, it is increased due to the release of leptin, cytokine, and other inflammatory factors by adipose tissue. Our study also showed a clear relationship between overweight and high levels of TSH (25). Medici *et al.* demonstrated higher BP in mothers with hyperthyroidism in the Netherlands. However, no relationship was found between hypothyroidism and hypertension. Nevertheless, our results showed higher diastolic BP in hypothyroidism women, which contradicted the results reported by Medici *et al.* (26).

The present study findings revealed that hypothyroidism increased the prevalence of high diastolic BP by 0.04. Moreover, this study indicated that hypothyroidism in obese people significantly increased BP. A variety of factors, such as stress, consumption of supplements, diet, racial differences, and lifestyle affect BP and can justify the differences in results (27-29).

The results of this study were congruent with the data presented by Ashoor *et al.* in Spain. In this study, the prevalences of hypertension and preeclampsia were five times higher in women with high TSH, compared to individuals with normal TSH. Although our study did not find a significant relationship between hypothyroidism and preeclampsia, elevated diastolic BP was found in this group. We observed that an increase in the diastolic BP of pregnant mothers augmented the abortion rate by 1.042 (30).

A meta-analysis conducted by Metwally *et al.* in England indicated a higher risk of spontaneous abortion in obese women (10). However, the present study did not reveal any significant relationship between obesity, weight gain, and abortion.

A direct relationship was found between diastolic BP and abortion in our investigation as overweight caused a rise in systolic and diastolic BPs in women with hypothyroidism. It could be concluded that hypothyroidism, which results in overweight, obesity, and hypertension can affect abortion. The controversy between our results and the findings of Metwally *et al.* could be attributed to the difference in sample size and factors that affect abortion. It should be noted that our study just investigated abortion, not a recurrent miscarriage (10).

In our study, in line with the study of Azizi *et al.* in Iran, the results showed that hypothyroidism in pregnancy is associated with gestational hypertension and abortion (31). The findings of a retrospective study in Saudi Arabia showed the adverse effects of hypothyroidism on the fetus and mother. Given that, the relationship between maternal hypothyroidism and infant death has been reported, the results of the mentioned study could be consistent with our findings as both have reported an increased risk of miscarriage in hypothyroid pregnant women with high diastolic BP (6).

A study by Sahila *et al.* in India demonstrated that TSH level and obesity were significantly higher in pregnant women with hypertension in the third trimester of pregnancy, compared to the control group. Although our results were for the first trimester of pregnant women with hypothyroidism, these data are in line with the correlation reported between hypothyroidism, hypertension, and overweight in pregnant women (32).

In our previous studies on preeclampsia, we indicated that diastolic BP augmented in preeclampsia cases. These results may be the reason for increased preeclampsia in these women due to the elevation in diastolic BP in pregnant women with hypothyroidism. However, there was no difference in the amount of excreted protein (17, 18).

## Conclusion

According to the results and the impact of hypothyroidism on BMI, it may be concluded that overweight in women with hypothyroidism can affect abortion by causing high diastolic BP. Therefore, it is expected that the risk of hypothyroidism reduces in these women through a weight control program leading to the ensured health of both mother and fetus.

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## Conflict of Interest

Authors declared that they have no conflicts of interest.

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