

Original Article

Association of Maternal Hypothyroidism with Pre-eclampsia

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ABSTRACT

Background and Objective: Hypertensive disorders complicating pregnancy are common and from one of the deadly triad, along with hemorrhage and infection that contribute greatly to prenatal and maternal morbidity and mortality in the developing countries. This study was designed to investigate the relationship between maternal hypothyroidism and pre-eclampsia.

Materials and Methods: In a prospective case-control study, maternal thyroid hormonal status was evaluated in 132 pregnant women with gestational hypertension and compared to controls.

Results: It was found out that 23 women (7.3%) had pregnancy-induced hypertension (PIH), 45 women (14.3%) had mild pre-eclampsia, 62 women (19.7%) had severe pre-eclampsia and 2 (0.6%) had eclampsia. Mean of thyroid stimulating hormone (TSH) levels was not significantly higher in pre-eclamptic group as compared to controls ($p>0.05$).

Conclusion: Maternal hypothyroidism might not be associated with pre-eclampsia.

Key words: Pre-eclampsia, Hypothyroidism, Pregnancy

Introduction

Hypertensive disorders complicating pregnancy are common and from one of the deadly triad, along with hemorrhage and infection, that contribute greatly to prenatal and maternal morbidity and mortality in the developing countries (1;2). Despite decade of intensive research, how pregnancy incites or aggravates hypertension remains unsolved (2). The physiological changes in the thyroid gland during pregnancy are well-understood but only a few reports provide information about thyroid function in complicated pregnancies (3). Although pregnancy is associated with mild hyperthyroxinemia, pre-eclamptic women have high incidence of hypothyroidism (4-

6). On the other hand, pre-eclampsia has been also observed in 16.7% of subclinical and 43.7% of overt cases of hypothyroidism during pregnancy (7). A recent report on 27 women with severe pre-eclampsia from Jordan found that there was no significant difference in the levels of TSH between the pre-eclamptic patients and healthy controls (8). Ashok et al showed that mean serum TSH levels were significantly increased without concomitant changes in free T3 and thyroxin in pre-eclampsia as compared to normal pregnancy. They suggested that abnormal TSH titers might be associated with a risk for occurrence of pre-eclampsia (3). The aim of this study is to evaluate the association between hypothyroidism and pre-eclampsia.

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Materials and Methods

One hundred thirty two hypertensive pregnant women with gestational age more than 20 weeks referred to gynecology and obstetrics center of University enrolled in a prospective case-control study during the years 2002-2004. The inclusion criteria were measurement of two elevated blood pressures more than 140/90 mmHg at least 6 h apart with or without proteinuria (which was diagnosed when a reading of +1 or more on the dipstick was found in repeated clean catch midstream urine sample) (9), age between 18 and 40 years, no previous history of thyroid disease, non-molar and non-multiple gestation, and no previous history of congenitally malformed fetus. One hundred eighty two of age (± 1 year) and gestation (± 1 week) matched healthy normotensive pregnant women constituted the control group. The development of hypertension any time during antenatal follow-up excluded them from the control group. The exclusion criteria for both groups were a history of hypertension, history of any metabolic disorder before or during the pregnancy, and a history of intake of any medication that might affect thyroid function and history of renal disease.

Informed consent was obtained from each woman. Then, 2 ml venous blood sample was taken from the cubital vein of hypertensive women after the diagnosis was made but before the initiation of the antihypertensive treatment and before the delivery and each control subject as mentioned above. All samples were sent to the laboratory with different code numbers which were deciphered at the time of the analysis of data. Sera was separated and stored at -20 °C until assayed. Thyroid stimulating hormone was measured using radioimmunoassay (RIA, Pouyesh Tashkhis, Tehran, Iran). All women were followed up through their antenatal, intrapartum and postpartum period.

Data were analyzed using SPSS and statistical comparisons between two groups were performed using χ^2 test.

Results

A total of 314 pregnant women were recruited in this case-control study. Of these, in the case group, 23 women (7.3%) had pregnancy-induced hypertension (PIH), 45 women (14.3%) had mild pre-eclampsia,

62 women (19.7%) had severe pre-eclampsia and 2 (0.6%) had eclampsia. The mean (\pm SD) age of the study group and control group was 27.4 ± 5.24 years and 26.3 ± 4.7 years respectively and there was no statistically significant difference between the two groups ($p > 0.05$). The values of TSH levels in the two groups are shown in Table 1. The mean values of thyroid hormones were within the normal laboratory reference ranges in both groups. The mean TSH levels were not significantly higher in pre-eclamptic group as compared to controls ($p > 0.05$). In the case group, in women who had hypothyroidism (8 cases), 2 had mild pre-eclampsia and 6 had severe pre-eclampsia. Out of 314 pregnant women in this study, 8(6.06%) women in the pre-eclamptic study group and 8(4.39%) in the control group had abnormal TSH titers (> 5 mIU/ml). This difference between the two groups is not found to be statistically significant ($p > 0.05$).

Table 1: TSH levels in studied women with pre-eclampsia and in control group

	Normal Range	Studied group mean \pm SD	Control group mean \pm SD
*TSH (mIU/ml)	3.0-5.0	3.8 ± 2.1	2.2 ± 2.01
p > 0.05*			

Discussion

In this study, mean TSH is not significantly increased in pre-eclamptic patients at the time of diagnosis as compared to control subjects. Free T3 and free T4 were comparable in both groups. Our findings supported the reports that pre-eclamptic women had not a higher incidence of biochemical hypothyroidism compared with normotensive pregnant women. A recent report of 27 women with severe pre-eclampsia from Jordan found that there was no significant difference in the levels of FT4, FT3 and TSH between the pre-eclamptic patients and healthy controls in the various gestational age subgroups (8). Wolfberg AJ found that women with hypothyroid disease were more likely to have chronic hypertension (2.3% vs. 1.2%, $p = 0.03$) and had an increased risk of pre-eclampsia (4.3% vs. 2.6%, $p = 0.03$) as compared to women without thyroid disease (10). Kumar et al showed that mean serum TSH levels were significantly increased

without concomitant changes in free T3 and T4, in pre-eclampsia compared to normal pregnancy (3).

Pre-eclampsia is a well-defined clinical entity affecting pregnant women, the etiology of which remains uncertain. Recently, the relationship between thyroid dysfunction and pre-eclampsia has been reported (3;10). Mild alteration in the thyroid hormones might occur due to non-thyroidal illness acting as a stress factor as well as due to decreased plasma albumin concentrations in these patients (11;12). Serum total T3 (TT3) and TT4 were significantly decreased and TSH was significantly increased in pre-eclamptic women in their third trimester (4-6;13;14). Higher levels of FT4 and TT4 along with lower levels of TT3 and FT3 were observed in toxemic patients compared to normal pregnant women (13). The titers of FT3 are reported to be significantly related to the decreased plasma albumin concentration in pre-eclamptic women (5). Modest decreases in thyroid hormones with concomitant increases in TSH levels in maternal serum correlated with severity of pre-eclampsia or eclampsia and high levels of endothelin. The endothelial cell dysfunction plays an important role in the pathogenesis of pre-eclampsia. Nitric oxide, a vasodilator released from the endothelial cells, regulates secretion of thyroid hormones by modulating regional blood flow in an animal study (13). Reduced serum concentrations of thyroxine binding globulin (TBG), T3 and T4 may also be explained by the faulty estrogen production due to placental dysfunction in pre-eclamptic women. FT4 concentration is not related to plasma albumin (5). The findings of our study regarding normal thyroid function test may be due to the fact that the blood sample was taken just at the time of diagnosis of pre-eclampsia. It is possible that low titers of T3 and T4 along with high TSH titers would be observed at a later stage of pre-eclampsia (i.e. with severe disease and low plasma albumin levels). In addition, TT4, TT3, serum albumin and thyroid antibodies were not measured in studied women.

Conclusion

The association between thyroid function and pre-eclampsia needs further investigation because of the small number of subjects in this study. A multi-centric study may answer the association and mechanism of thyroid abnormality in pre-eclamptic women in terms

of the geographical variation. Therefore, according to our findings, identification of thyroid abnormalities might not be associated with pre-eclampsia.

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