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Serum Thyroid Hormone Levels in Preeclampsia Women in Gorgan

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Etiology of preeclampsia is clearly unknown. The aim of this study was to assess thyroid hormone levels in mild and severe preeclampsia women and compare them with healthy pregnant women. This study was done on 50 healthy pregnant and 50 preeclampsia women in the third trimester in the Sayyad Shirazi educational Hospital, Gynecology Department of Golestan University of Medical Sciences, Iran, 2014. There were significant differences in T4 level among mild preeclampsia and healthy pregnant women. There were also significant differences in T4 and T3 levels between severe, mild preeclampsia women and healthy pregnant women. We observed a significant positive correlation between systolic and diastolic blood pressure and thyroid hormones. Serum T3 and T4 levels were significantly increased with development of preeclampsia. There is association between thyroid hormone abnormalities and hypertension. The difference of our study with other findings could be related to different geographical areas, races and diets. Variation of thyroid functioning later in life may develop in preeclampsia women. Thus, it suggests that thyroid function test may necessary to screen preeclampsia women during pregnancy and after parturition.

Key words: Thyroid hormones, preeclampsia, gorgan

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INTRODUCTION

There are an association between preeclampsia and a high incidence of maternal and fetal mortality (Cunningham *et al*., 2010). Preeclampsia happens after 20 weeks pregnancy and shows various disorders such as hypertension, edema and proteinuria (Pankaj *et al*., 2008). Liver, kidney and brain are the most affected organs in preeclampsia women (Duha and Konar, 2001). It is reported that preeclampsia influences 0.4-2.8% of all pregnancies in developed and developing countries (Villar *et al*., 2003). The most risk of preeclampsia usually occurs in women younger than 20 years (Brooks, 2005). Prevalence of preeclampsia is seen more in developing countries. This can be because of poverty, malnutrition, micronutrient deficiencies, early marriage, early child birth and lack of antenatal care (Khatoon, 1992). Many studies indicated a relationship between of thyroid hormone levels and development and severity of preeclampsia (Raoofi *et al*., 2014). Etiology of preeclampsia is not completely clear. Studies on preeclampsia patients have been revealed that 16.7 and 43.7% of subjects were sub-clinical and overt cases of hypothyroidism during pregnancy (Davis *et al*., 1988). There is usually an association between pregnancy and very mild hyperthyroxinemia. Preeclampsia women show high incidence of hypothyroidism that might correlate with the severity of preeclampsia (Lao *et al*., 1988, 1990; Kaya *et al*., 1994). Different studies have shown that mean serum TSH (thyroid-stimulating hormone) were significantly elevated and free T3 (triiodothyronine) and T4 (thyroxin) were without alterations in preeclampsia women (Kumar *et al*., 2005) whereas other studies showed increased level of TSH and decreased levels of T3 and T4 in preeclampsia women in comparison with normal pregnant (Mostaghel *et al*., 2008; Kharb *et al*., 2013; Raoofi *et al*., 2014). Some investigators reported no change in serum TSH in pregnancy, while some found significant increases in TSH during pregnancy. Ashoor *et al*. (2010) showed serum TSH increased whereas T3 and T4 decreased with gestational age. Some other study showed that serum levels of free T4 and TSH were increased in women with severe preeclampsia when compared with mild preeclampsia and normal pregnancy (Larijani *et al*., 2004). Studies have shown that hypertensive disorders may cause of maternal and fetal morbidity and mortality. There are many other complications such as renal failure, disseminated intravascular coagulation, cerebrovascular bleeding, intrauterine growth retardation, abruption placenta, premature delivery and stillbirths that may cause also maternal and fetal morbidity and mortality (Duley, 2009; Steegers *et al*., 2010). Some findings have indicated an elevated risk of hypertensive disorders in mothers with hypothyroidism (Ashoor *et al*., 2010; Mannisto *et al*., 2013; Wilson *et al*., 2012) or hyperthyroidism (Mannisto *et al*., 2013), while some of other studies did not show any associations (Casey *et al*., 2005; Cleary-Goldman *et al*., 2008; Karakosta *et al*., 2012; Mannisto *et al*., 2010). Most of these studies did not control some factors like thyroid autoimmunity, smoking, Body Mass Index (BMI), ethnicity, socioeconomic status and parity. Many studies have revealed that a small change in function of thyroid can affect on pregnancy complications (Medici *et al*., 2013; Shields *et al*., 2011; Taylor *et al*., 2013). Some recent studies indicated that a little change in thyroid function can influence on complications of pregnancy (Medici *et al*., 2013; Shields *et al*., 2011; Taylor *et al*., 2013). It is reported that women with preeclampsia may show an increased risk for decreased thyroid functioning later in life (Levin *et al*., 2009). Therefore, the aim of this study was to assess thyroid hormones in mild and severe preeclampsia women and healthy pregnant women.

MATERIALS AND METHODS

This study was done on 50 healthy pregnant and 50 preeclampsia women in the third trimester in the Sayyad shirazi educational Hospital, Gynecology Department of Golestan University of Medical Sciences, Iran, 2014. The study was approved by Ethical Committees of the Research Deputy of University of Medical Sciences Systolic and diastolic blood pressure was measured by using a standard mercury manometer with women in sitting position, from their right hands. Definition of 1-preeclampsia (n = 50), 2-mild preeclampsia (n = 35) and 3-severe preeclampsia (n = 15) women were as follow:

- A blood pressure higher than 130/85 mmHg and proteinuria with 1+or greater by dipstick
- A blood pressure higher than 160/110 mmHg or proteinuria with 1+-3+by dipstick
- A blood pressure higher than 160/110 mmHg or proteinuria greater than 3+by dipstick (Bolte *et al*., 2001)

Preeclampsia was diagnosed by a gynecologist. All three groups were age, body mass index and gravidity matched. Blood pressure higher than 140/90 mmHg on at least two occasions 6 h apart and/or proteinuria were inclusion criteria for preeclampsia women (Weinstein, 1982). Healthy pregnant group had T3 (triiodothyronine), T4 (thyroxine) and TSH (thyroid-stimulating hormone) values and blood pressure within normal range. Our exclusion criteria were history of diabetes mellitus, chronic hypertension, renal, cardiovascular, liver disease, endocrine disorder, any

chronic illness, twin pregnancies, preexisting thyroid disease, thyroid medication usage and fertility treatment. Ten milliliter blood sample was provided from all subjects. T3, T4 and TSH were measured using commercial kits and Elisa (Model: Statfax-2100, USA). The results were shown in Mean±standard deviation. Statistical analyze of data was carried out by SPSS-16 version. Comparison of thyroid hormones between preeclampsia (mild and severe) and healthy women (differences between groups) was performed using independent sample t-test. Correlations between parameters were done by Pearson correlation test. p-value<0.05 was considered significant.

RESULTS

Fifty woman with the diagnosis of preeclampsia and 50 healthy pregnant women were taken part in this study. The mean age of the preeclampsia and healthy pregnant women were 26.54±3.74 and 26.47±4.50 years, respectively.

The mean gestational age was 31.24±3.49 and 30.17±3.10 weeks in preeclampsia and healthy pregnant women. The mean TSH of preeclampsia and healthy pregnant women were 2.30±1.47 and 1.82±1.32 μIU dL^{-1}, respectively and there was no significant difference between the two groups (p = 0.097). The mean T4 of preeclampsia and healthy pregnant women were 5.03±3.04 and 5.02±2.01 μg dL^{-1}, respectively and there was no significant difference between the two groups (p = 0.98).

The mean T3 of preeclampsia and healthy pregnant women were 4.0±1.45 and 3.90±1.26 μg dL^{-1}, respectively and there was no significant difference between the 2 groups (p = 0.74) (Table 1). No significant differences were considered in TSH and T3 levels among mild preeclampsia and healthy pregnant women but there were significant differences in T4 level (p = 0.005).

There are significant differences in T4 and T3 levels when severe, mild preeclampsia women and healthy pregnant women with each other (Table 2). Correlations between thyroid hormones and systolic and diastolic blood pressure are shown in Table 3. We observed a significant positive correlation between systolic and diastolic blood pressure and thyroid hormones. There were no correlations between TSH and systolic blood pressure.

DISCUSSION

Different factors may play an important role in development of preeclampsia. Etiology of preeclampsia is clearly unknown and it may happen at second or third trimester of pregnancy (Mehdi *et al*., 2009; Hasanzadeh *et al*., 2008). Some studies showed an association between the levels of thyroid hormones and development of preeclampsia. In present study, our findings showed that levels of TSH and T3 were higher in preeclampsia women and no changes in the level of T4 in preeclampsia women compared to healthy pregnant women (p>0.05) which was not in agreement with the finding of other study (Kumar *et al*., 2005; Lao *et al*., 1990; Skjoldebrand *et al*., 1986; Basbug *et al*., 1999). Several studies showed that there are a significant association between thyroid hormones and the development and severity of preeclampsia (Ipadeola *et al*., 2013; Osathanondh *et al*., 1976; Raoofi *et al*., 2014; Kumar *et al*., 2005). Various other studies with different findings are available with relation to T4 (Low and high levels of T4) and TSH levels (High levels of TSH) in preeclampsia women (Kumar *et al*., 2005; Tolino *et al*., 1985; Raoofi *et al*., 2014). Some studies have shown that there were no significant differences in TSH levels between preeclampsia and healthy women which is in agreement with our results (Qublan *et al*., 2003; Khaliq *et al*., 1999). In the present study, T4 level was significantly lower in mild preeclamptics when compared with healthy pregnant women (p<0.05), who are in agreement with findings of other studies (Qublan *et al*., 2003; Levin *et al*., 2009). Severe preeclampsia women showed significantly higher T4 and T3 levels compared to healthy ones (p = 0.0001 and p = 0.001). Qublan *et al*. (2003) showed that the thyroid function is not changed in severe preeclampsia. The increased level of TSH (not significant) in preeclampsia women shows an association with the risk for developing and severity of preeclampsia (Mostaghel *et al*., 2008). Many studies indicated that preeclampsia women showed significantly increased or no significant elevation level of TSH (Khaliq *et al*., 1999; Sardana *et al*., 2009). This alteration may occur as a result of association of increased level of TSH with thyroid peroxidase antibodies (Kaya *et al*., 1994). Thyroid dysfunction may change thyroid hormone secretion which can significantly increase T3 and T4 levels in severe

Table 1: Clinical and biochemical characteristic of preeclampsia and healthy pregnant women

Parameters	Women with preeclampsia	Healthy pregnant women	p-value
No. (%)	50.00	50.00	
Maternal age (years)	26.50±3.90	27.10±4.60	0.449
Gestational age (weeks)	31.24±3.49	30.17±3.10	0.355
Hypertensive (%)	100.00	-	-
TSH (μIU dL^{-1})	2.30±1.47	1.82±1.32	0.097
T4 (μg dL^{-1})	5.03±3.04	5.02±2.01	0.980
T3 (μg dL^{-1})	4.00±1.45	3.90±1.26	0.740

Table 2: Clinical and biochemical characteristic of women with mild and severe preeclampsia and healthy pregnant women

Parameters	Women with mild preeclampsia	Healthy pregnant women	p-value	Women with severe preeclampsia	Healthy pregnant women	p-value	Women with severe preeclampsia	Women with mild preeclampsia	p-value
No. (%)	35.00 (70)	50		15.00 (30)	50		15.00 (30)	35.00 (70)	
Maternal age (years)	27.00±4.11	27.10±4.60	0.843	25.41±3.50	27.10±4.60	0.369	25.41±3.50	27.00±4.11	0.434
Gestational age (weeks)	31.47±3.66	30.17±3.10	0.848	28.75±8.69	30.17±3.10	0.813	28.75±8.69	31.47±3.66	0.892
TSH (μ IU dL^{-1})	2.30±1.50	1.82±1.30	0.271	2.27±1.37	1.82±1.30	0.539	2.27±1.37	2.30±1.50	0.435
T4 (μg dL^{-1})	3.57±2.07	5.02±2.01	0.005	8.44±2.06	5.02±2.01	0.0001	8.44±2.06	3.57±2.07	0.0001
T3 (μg dL^{-1})	3.46±1.20	3.90±1.26	0.227	5.25±1.21	3.90±1.26	0.001	5.25±1.21	3.46±1.20	0.0001

Table 3: Correlation of thyroid hormones with systolic and diastolic and blood pressure

Parameters	TSH	T4	T3
Systolic blood pressure	R = 0.174	P = 0.084	R = 0.216
	P = 0.031	R = 0.198	P = 0.048
Diastolic blood pressure	R = 0.206	P = 0.039	R = 0.296
	P = 0.003	R = 0.205	P = 0.041

preeclampsia women. These findings were inconsistent with some other studies (Kumar *et al*., 2005; Pasupathi *et al*., 2009; Casey *et al*., 2005). A study has indicated that there are a correlation between alterations in thyroid hormone levels and occurrence and severity of morbidity and mortality of preeclampsia women. It has shown that TSH levels of 5 μ IU mL^{-1} cause to a higher risk of development of preeclampsia (Qublan *et al*., 2003). Severe preeclampsia women showed significantly higher T4 and T3 levels compared to mild ones (p = 0.0001 and p = 0.0001). This means that with development of preeclampsia from mild to severe, thyroid dysfunction may occur in preeclampsia women. This may cause by pathological alterations and unusual secretion of thyroid tissue that may influence on T3 and T4 synthesis and secretion. The mechanism of thyroid hormone alterations is not exactly clear in preeclampsia women. There are many suggestions such as endothelial dysfunction, decreased alteration of T4 to T3 and placental dysfunction can show an important role in pathogens of preeclampsia (Kumar *et al*., 2005). We also studied the associations between thyroid hormones and high systolic and diastolic blood pressure levels in preeclampsia women. There were statistically significant associations between systolic blood pressure with T3 and T4 levels and diastolic blood pressure with TSH, T3 and T4 levels. These findings were in agreement with several studies (Larijani *et al*., 2004; Karakosta *et al*., 2012; Luewan *et al*., 2011; Mannisto *et al*., 2013, 2010; Sahu *et al*., 2010; Wilson *et al*., 2012), while, other studies did not show any associations between above mentioned parameters (Karakosta *et al*., 2012; Luewan *et al*., 2011; Sahu *et al*., 2010). Many studies have indicated that hypertensive disorders may elevate risk of maternal hypertension, ischemic heart disease, stroke, renal disease and mortality (Bellamy *et al*., 2007; Vikse *et al*., 2008; Williams, 2011). Thyroid hormone may affect hypertensive disorders onset in pregnant women. Increased level of thyroid hormone can cause endothelial cell dysfunction, which has an important role in the pathophysiology of hypertensive disorders during pregnancy (Steegers *et al*., 2010). Developed prediction model suggested by Poon *et al*. (2009). The model contains maternal history, uterine artery pulsatility index; mean arterial pressure, pregnancy-associated plasma protein-A and placental growth factor (Poon *et al*., 2009). It can suggest that the use of thyroid function test is practical for diagnose of thyroid function.

CONCLUSION

The results of the present study suggest that there were no significant different in T3, T4 and TSH levels between preeclampsia and healthy pregnant women, but serum T3 and T4 levels were significantly increased with development of preeclampsia. There is association between thyroid abnormalities and pregnancy caused hypertension. The difference of our study with other findings could be related to different geographical areas, races and diets. Variation of thyroid functioning later in life may develop in preeclampsia women. Thus, it suggests that thyroid function test may necessary to screen preeclampsia women during pregnancy and after parturition.

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