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Maternal Thyroid Function Tests between 11 and 13 Weeks of Pregnancy as a Predictor of Preeclampsia

HOSSAM ELDIN F. ABD EL RAHIM, M.D.*; ABD EL MONSEF A. SEDEEK, M.D.*;
AHMED F. ABD EL AZEZ, M.D.** and MOHAMED K. ABD EL HADY, M.Sc.*

The Departments of Obstetrics & Gynaecology and Clinical Pathology**, Faculty of Medicine, Al-Azhar University*

Abstract

Background: Thyroid dysfunction is one of the commonest endocrine disorders encountered during pregnancy after diabetes mellitus. Pregnancy develops major changes in hypo thalamic pituitary thyroid axis, iodine metabolism and the immune function. Thyroid physiology alters in order to meet increased metabolic demands in pregnancy. Pre-eclampsia is much more common in women who are pregnant for the first time. Women who have previously been diagnosed with pre-eclampsia are also more likely to experience pre-eclampsia in subsequent pregnancies.

Aim of Study: The aim of this study was to identify the prognostic value of thyroid function tests between 11 and 13 weeks of pregnancy as predictor of preeclampsia occurrence.

Patients and Methods: This study was a prospective observational (cohort) study. This study was done in Obstetrics & Gynaecology Department, Shubrakhet Hospital From Jan. 2021 – Oct. 2021. Subjects was women attending for their routine first hospital visit in pregnancy, which is held at 11^{+0} to 13^{+6} weeks of gestation and followed-up until delivery.

Results: The results of our study showed that there was no significant difference between the two studied groups (preeclampsia and normal pregnant group) regarding maternal age, BMI, gestational age. The blood pressure was significantly high in preeclampsia group. The incidence of Hypothyroidism was significantly higher in preeclampsia group (63.3% more than the normal pregnant group (18.3%).

Conclusion: The results of the present study showed that there were a significant different in T3, T4 and TSH levels between preeclampsia and healthy pregnant women. There was association between thyroid abnormalities and pregnancy caused hypertension.

Key Words: *Thyroid dysfunction test – Predictor of preeclampsia – Pregnancy.*

Introduction

PREECLAMPSIA (PE) is a disorder of pregnancy characterized by high blood pressure and often a significant amount of protein in the urine. When it arises, the condition begins after 20 weeks of pregnancy **[1]**.

In severe disease there may be red blood cell breakdown, a low blood platelet count, impaired liver functions, kidney dysfunction, swelling, shortness of breath due to fluid in the lungs, or visual disturbances. Pre-eclampsia increases the risk of poor outcomes for both the mother and the baby. If left untreated, it may result in seizures at which point it is known as eclampsia **[2]**.

It affects about 2% of pregnancies, is a major cause of maternal and perinatal morbidity and mortality **[1]**.

Pre-eclampsia is much more common in women who are pregnant for the first time. Women who have previously been diagnosed with pre-eclampsia are also more likely to experience pre-eclampsia in subsequent pregnancies. Pre-eclampsia is also more common in women who have pre-existing hypertension, obesity, diabetes, autoimmune diseases such as lupus, various inherited thrombophilias such as Factor V Leiden mutation, renal disease, multiple gestation (twins or multiple birth), and advanced maternal age **[3]**.

Recent evidence suggests that PE can be divided into early PE requiring delivery before 34 weeks, and late PE with the former, being associated with a high incidence of fetal growth restriction, whereas in late PE fetal growth is usually normal **[4]**.

The underlying mechanism for the development of PE is thought to be impaired trophoblastic invasion of the maternal spiral arteries and their conversion from narrow muscular vessels to wide non-muscular channels independent of maternal vasomotor control **[5]**.

Correspondence to: Dr. Hossam Eldin F. Abd El Rahim, The Department of Obstetrics & Gynaecology, Faculty of Medicine, Al-Azhar University

Several studies have reported that in patients presenting with the clinical features of PE, thyroid function is disturbed with increase in maternal serum thyroid stimulating hormone (TSH) and decrease in the levels of thyroid hormones **[6]**.

The results of a population based study in which serum TSH was measured in women on average 20 years after their first pregnancy highlighted further the interrelation between hypothyroidism and PE **[7]**.

The aim of this study was to identify the prognostic value of thyroid function tests between 11 and 13 weeks of pregnancy as predictor of preeclampsia occurrence.

Patients and Methods

This Study was prospective observational (cohort) study, it was done in Obstetrics & Gynaecology Department, Shubrakhet Hospital from Jan. 2021 – Oct. 2021, subjects was women attending for their routine first hospital visit in pregnancy, which is held at 11^{+0} to 13^{+6} weeks of gestation and followed-up until delivery.

Inclusion criteria: Women attending for their routine first hospital visit in pregnancy which is held at 11^{+0} to 13^{+6} weeks of gestation, their ages from18 to 35 years and Singleton pregnancy.

Exclusion criteria: History of thyroid disease and pre-existing medical disorders.

All the participating patient was subjected to: Full detailed history, blood pressure, automated measurement, ultrasound scan.

Investigations: Samples from y 5oo pregnant women was taken at 11 to 13 weeks of pregnancy and then will be stored frozen at (–20ºC to –25ºC.). Samples of women who was developed pre-eclampsia was analyzed for serum concentrations of free triiodothyronine (FT3), free thyroxine (FT4), TSH, total triiodothyronine (Total T3) and total thyroxine (Total T4) which was taken at 11 to 13. Other comparative samples of women who was not developed pre-eclampsia was analyzed for same hormones levels.

Results

Table (1) shows that there was no statistical significant difference between the two studied groups regarding age, BMI, and gestational age (p>0.05), while there was statistical significant difference regarding systolic and diastolic blood pressure (p<0.05).

Table (2) shows that there was statistical significant difference between the two studied groups regarding TSH (p<0.05). There was statistical significant difference between the two studied groups regarding total and free triiodothyronine (p<0.05). There was statistical significant difference between the two studied groups regarding total and free thyroxine (p<0.05). There was statistical significant difference between the two studied groups regarding hypothyroidism (p<0.05).

Table (1): Comparison between the two studied groups regarding age, BMI, gestational age, systolic blood pressure and diastolic blood pressure.

	Preeclampsia	Normal control	*t* *p*
Age (Mean ± S.D.)	26.55±3.92	25.11±3.10	1.62 0.088
BMI (Mean ± S.D.)	30.90±3.78	31.53±4.16	1.26 0.168
Gestational age (Mean ± S.D.)	12.07±0.78	12.13±0.77	0.79 0.319 N.S.
Systolic blood pressure (Mean ± S.D.)	153.88±7.26	114.50±5.86	5.65 0.003*
Diastolic blood pressure (Mean ± S.D.)	103.68±6.59	80.65±3.32	4.98 0.004*

Table (2): Comparison between the two studied groups regarding TSH, total and free triiodothyronine, total and free thyroxine, and hypothyrodism.

	Preeclampsia	Normal control	*t* *p*
- TSH (mIU/L) (Mean ± S.D.)	2.58±1.47	1.45±0.94	6.01 0.001*
- Free triiodothyronine (FT3) (pmol/L) (Mean ± S.D.)	3.51±0.54	3.97±0.45	2.66 0.027*
- Free thyroxine (FT4) (pmol/L) (Mean ± S.D.)	11.34±2.30	12.83±1.57	3.25 0.020*
- Total triiodothyronine (Total T3) (nmol/L) (Mean ± S.D.)	0.96±0.55	1.53±0.58	3.36 0.004*
- Total thyroxine (Total T4) (nmol/L) (Mean ± S.D.)	110.91±27.29	104.87±31.08	1.13 0.130 N.S.
Hypothyroidism	No. %	No. %	
Yes	38 63.3	11 18.3	4.68
No	22 36.7	49 81.7	0.013*

Discussion

This study was a prospective observational (cohort) study. This study was done in Obstetrics & Gynaecology department Shubrakhet Hospital. Subjects were women attending for their routine first hospital visit in pregnancy, which is held at 11^{+0} to 13^{+6} weeks of gestation and followed-up until delivery.

The results of our study showed that there was no significant difference between the two studied groups (preeclampsia and normal pregnant group) regarding maternal age, BMI, gestational age. The blood pressure was significantly high in preeclampsia group. The incidence of Hypothyroidism was significantly higher in preeclampsia group (63.3% more than the normal pregnant group (18.3%).

In agreement with our study, Lintula et al. **[8],** study the Hypothyroidism and the increased risk of preeclampsia, they found that there was a significant association between hypothyroidism and incidence of preeclampsia **[8]**.

There have been only a few similar studies investigating the association between preeclampsia and hypothyroidism in pregnant women during the last decade. Similar data have emerged from earlier studies, but no separate evaluation of maternal characteristics or type of hypothyroidism has been reported previously **[9]**.

In studies, it has been reported that women using levothyroxine have a higher occurrence of preeclampsia, varying between 4% and 7%. In addition, maternal high TSH-levels during pregnancy have been associated with the development of preeclampsia in one retrospective cross-sectional and one prospective cohort study **[10]**.

However, we observed that neither the dose of levothyroxine medication nor maternal serum levels of TSH were associated with the development of preeclampsia in women who had used levothyroxine during pregnancy **[10]**.

Also in agreement with our results, Banik et al. **[11]**, study the thyroid dysfunction in preeclampsia and related fetomaternal outcomes, they found that a total of 95 preeclamptic patients were studied in the present study; out of which 42 (44.2%) were found to have thyroid dysfunction with 37 (38.9%) patients having subclinical hypothyroidism and 4 (4.2%) patients with overt hypothyroidism and 1 (1%) hyperthyroidism **[11]**.

Bankowska et al. **[12]** found that 78.2% of patients with pregnancy induced hypertension had thyroid dysfunction and concluded that subclinical hypothyroidism as the most common thyroid dysfunction in the tested group supporting the findings of the present study **[12]**.

Kharb et al. **[13]** also observed that 55% of preeclamptic patients had hypothyroidism **[13]**. Deshpande et al. **[14]** also found that there was a significant association between preeclampsia and thyroid hypofunction (p=.0406). However, contrary to this, thyroid function changes were not found in preeclamptic patients in the study of Khadem M et al. **[15]**.

Severe preeclampsia was seen in 64.3% of the patients with thyroid dysfunction compared with 39.6% in the euthyroid patients which was found to be statistically significant.

Similarly, Kharb et al. **[13]** and Wilson et al. **[15]** found a significant association between severity of preeclampsia and hypothyroidism. Kharb S et al., also found that preeclamptics with raised TSH levels had significantly higher mean arterial pressure as compared with preeclamptic patients with normal TSH levels (p<.001) **[13,15]**.

There are a number of observations that support the biological plausibility of this association. These include the cardiovascular effects of abnormal concentration of thyroid hormones like ventricular hypertrophy leading to heart failure. These aberrations follow long term exposure to excessive or decreased thyroid hormones **[16]**.

Subclinical hypothyroidism might cause endothelial dysfunction characterised by diminished nitric oxide production with impaired vasorelaxation which might cause hypertension **[17]**.

Hypothyroidism might also cause vascular smooth muscle contraction, leading to increased diastolic hypertension, peripheral vascular resistance and decreased tissue perfusion **[18]**.

Sravani et al. **[19]** found that in hypothyroid women with hypertension, abruption was seen in 6%, IUD in 10% and IUGR in 14% of the patients supporting the findings of our study. These findings suggest that thyroid dysfunction in preeclampsia has a role to play in increasing the complications associated with it significantly needing timely detection and treatment for better outcomes **[19]**.

Kumar et al. **[20]** observed the similar findings in preeclamptic and eclamptic women with high TSH level and low thyroid hormones their finding suggested that preeclamptic women had higher incidence of biochemical hypothyroidism compared with normotensive pregnant women.20 It has been suggested that reduced concentration of thyroid hormones in preeclampsia may be due to the loss of protein-bound hormones in the urine **[21]**.

Lao et al. **[22]** reported decreased levels of FT4 and increased levels of TSH in preeclampsia. Abnormalities in placental function can interfere with oestrogen production that lead to decrease levels

of TBG, T3 & T4. Hypothyroidism can cause vascular smooth muscle contraction both in systemic and renal vessels, which leads to increased diastolic hypertension, peripheral vascular resistance, and decreased tissue perfusion **[22,23]**.

Thyroid dysfunction can be associated with proteinuria, which is known to result in increased excretion of thyroxine and thyroid-binding globulins. Endothelial activation/dysfunction is a central pathogenic feature in women with preeclampsia, which is a multiple system disorder during human pregnancy **[24]**.

Increased circulating VEGER-1 concentrationin preeclamptic women were associated with decreased circulating levels of free VEGF and PIGF, leading to an anti-angiogenic state and causing endothelial cell dysfunction **[25]**.

There is strong evidence that TSH can act as atissue specific angiogenesis in physiological and pathological conditions. Thus increases levels VEGF and TSH protein correlated with each other. TSH up regulates VEGF expression in vivo and vitro **[26]**.

Larijani et al., reported increased TSH levels and decreased free and total levels of T4 and T3 in a study of 39 pre-eclamptic patients compared to 42 healthy controls. These findings are in agreement with others in the literature **[27]**.

In contrast to our results, study the Maternal Thyroid Functions in Pre-Eclampsia, they found that there was no significant difference in the levels of FT3, FT4 and TSH between the pre-eclamptic group and normotensive controls in the third trimester of gestation. Their findings supported the report of Qublan et al. **[28]** who reported that thyroid function did not alter in severe pre-eclamptic women when compared with normotensive controls **[28]**.

On the other hand, data in the literature regarding TT4 levels are controversial. A few reports have observed lower TT4 levels in pre-eclampsia, while others have reported higher TT4 levels. Kumar et al. **[20]** and Sardana et al. **[29]** found high levels of TSH in pre-eclamptic patients, which lends support to earlier reports of a high incidence of biochemical hypothyroidism in pre-eclamptic women when compared with normotensive pregnant women **[20]**.

It has also been observed that pre-eclamptic women with higher TSH levels along with lower thyroid hormones were more likely to have small for gestational age newborns. TT3 and TT4 concentrations in pre-eclamptic and eclamptic women correlated positively with the birth-weight of their infants **[21]**.

Lao et al. **[22]** and Sardana et al. **[29]** observed a negative correlation between the birthweight of infants and TSH level in pre-eclamptic patients. In our study, a positive correlation between the birth-weight of the infant and thyroid hormones (TSH, FT3 and FT4) in pre-eclamptic patients was observed, although it was not statistically significant **[22,29]**.

The association of hypothyroidism and preeclampsia is not surprising, hypothyroidism being an accepted cause of reversible hypertension both in the pregnant and in the non pregnant population, as discussed elsewhere. Hypothyroidism can cause vascular smooth muscle contraction both in systemic and renal vessels, which leads to increased diastolic hypertension, peripheral vascular resistance, and decreased tissue perfusion **[30,23]**.

Thyroid dysfunction can be associated with proteinuria, which is known to result in increased excretion of thyroxine and thyroid-binding globulins. Rare cases, have been reported where proteinuria is severe enough to result in losses of thyroid-binding globulins and thyroxine that cannot be compensated by the body **[31]**.

Conclusion and Recommendation:

The results of the present study showed that there were a significant different in T3, T4 and TSH levels between preeclampsia and healthy pregnant women. There was association between thyroid abnormalities and pregnancy caused hypertension. 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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اختبار وظائف الغدة الدرقية فى الام بين ١١ و١٣ أسبو عا من الحمل كمتنبئ لحدوث تسمم الحمل

خلفية الدراسة : خلل الغدة الدرقية هو واحد من أكثر اضطرابات الغدد الصماء شيوعاً التى تصادف أثناء الحمل بعد داء السكرى. الحمل يتطور تغييرات كبيرة فى محور الغدة الدرقية الغدة النخامية تحت المهاد، واستقلاب اليود ووظيفة المناعة. يتغير فسيولوجيا الغدة الدرقية من أجل تلبية متطلبات التمثيل الغذائى المتزايدة فى الحمل. مقدمات الارتعاج أكثر شيوعاً لدى النساء الحوامل لأول مرة. النساء اللواتى تم تشخيصهن سابقاً بمقدمات الارتعاج هن أيضاً أكثر عرضة للإصابة بمقد مات الارتعاج فى حالات الحمل اللاحقة.

الهدف من الدراسة : كان الهدف من هذه الدراسة هو تحديد القيمة التنبؤية لاختبارات وظائف الغدة الدرقية بين ١١ و ١٣ أسبوعاً من الحمل كمؤشر لحدوث تسمم الحمل.

المرضى وطرق الدراسة : هذه الدراسة دراسة تنبؤية مستقبلية وأجريت فى قسم أمراض النساء والولادة مستشفى شبراخيت. حيث النساء يحضرن لزيارتهن الروتينية الأولى للمستشفى أثناء الحمل، والتى تقام بين ١١ إلى ١٣ أسبوع من الحمل ومتابعتها حتى الولادة.

تم حفظ العينات التى تم جمعها فى تلك الفترة من الحمل (١١ إلى ١٣ أسبوع) فى درجة حرارة −٢٠ إلى −٢٥ درجة مئوية حتى الولادة.

نتائج الدراسة : أظهرت نتائج الدراسة أنه لا يوجد فرق إحصائى بين المجموعتين المدروستين تسمم الحمل ومجموعة الحوامل الطبيعية فيما يتعلق بعمر الأم، مؤشر كتلة الجسم، عمر الحمل.

كان ضغط الدم مرتفعاً بشكل ملحوظ فى مجموعة تسمم الحمل.

كان معدل الإصابة بقصور الغدة الدرقية أعلى بشكل ملحوظ فى مجموعة تسمم الحمل (٦٣.٣٪) أكثر من مجموعة الحمل العادى (١٨.٣٪).

الاستنتاج : أظهرت نتائج هذه الدراسة أن هناك اختلافاً كبيراً فى مستويات T3 وT4 و TSH بين تسمم الحمل والنساء الحوامل الأصحاء. كان هناك ارتباط بين تشوهات الغدة الدرقية والحمل تسبب ارتفاع ضغط الدم.