Original Research Article

Evaluation of thyroid function test in severity of preeclampsia

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Abstract

Background: Maternal health and pregnancy outcome are noticeably affected when PE or more complicated conditions such as eclampsia. These syndromes substantially contribute to maternal morbidity and mortality. Maternal thyroid dysfunction during pregnancy has been shown to be associated with a number of adverse outcomes. The serum concentration of T4 and T3 may be different in PE than in normal pregnancy **Aim and objective :** To estimate thyroid function tests i.e. TSH, fT3 and fT4 levels in women with mild Preeclampsia and severe Preeclampsia **Methodology :** Total 120 pregnant women between 18 to 35 years studied. Data collected with pre tested questionnaire. Data included sociodemographic data, obstetric history, clinical examination of patients, thyroid function tests and birth weight of babies. Data analysed with appropriate statistical tests. **Results:** TSH is increased significantly with severity of preeclamptic women as compared to control. The fT3 decreases significantly with severity of PE as compared to control. The fT4 is increases but not significantly in PE as compared to control. TSH is correlated positively with systolic and diastolic B.P. and correlated negatively with birth weight in both mild and severe PE.

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INTRODUCTION

Common disorders of pregnancy are hypertensive disorders, gestational diabetes and premature birth[1]. Out of these, hypertensive disorders are the most common medical complications of pregnancy and are important cause of maternal and perinatal morbidity and mortality.[2]. PIH can be a serious and life threatening obstetric complication and is one of the most common cause of both maternal and neonatal morbidity resulting in an estimated 35-300 deaths per 1000 births[3]. PE may be further categorized as mild or severe. The patients with blood pressure ≥140/90 mmHg but <160/110 mmHg and proteinuria of ≥ 0.3 gm in 24 hrs which corresponds with 1+ or greater on a urine dipstick test without evidence of end-organ damage were included in mild PE[7]. A woman is considered to have severe PE when her blood pressure reading is ≥160 mm Hg systolic or ≥110 mm Hg diastolic; her proteinuria is ≥5 g of protein in the urine per 24 hours or 3+ or greater on two random urine samples collected at least 4 hrs apart or other organ systems are involved. She may have headache, visual disturbances, other CNS symptoms, pulmonary edema, cyanosis, abdominal pain or other cardiovascular symptoms[4].

PE is associated with increased risks of placental abruption, acute renal failure, cerebrovascular and cardiovascular complications, disseminated intravascular coagulation and maternal death. Hence, early diagnosis of PE and close observation are imperative[5]. During pregnancy, there is an increased thyroid demand and increased iodine uptake and synthesis of thyroid hormones[6]. In PE, the most affected organs are liver, kidneys and brain. Due to autointoxication, functional disorders in these organ systems are evident. As liver, kidneys, and muscles are the three main organs of peripheral deiodination of T4 to T3. There are limited numbers of studies on the levels of thyroid hormones in

pre-eclampsia and has been suggested that there may be an existence of mutual influences between pre-eclampsia and thyroid function[7]. The purpose of our study is to compare the levels of thyroid function tests in normotensive healthy pregnant women and women with PE between 28-40 weeks of gestation and also to correlate various demographic and biochemical parameters in studied groups and to study whether these parameters have any prognostic significance as in determing severity and as a predictor of adverse pregnancy outcome.

Aim and objective: To estimate thyroid function tests i.e. TSH, fT3 and fT4 levels in women with mild Preeclampsia and severe Preeclampsia

MATERIAL AND METHODS

It is a cross sectional study carried out in tertiary health institute in the department of biochemistry during period from March 2011 to August 2012. Total 120 pregnant women between 18 to 35 years visiting the gynecology and obstetrics OPD were included under study.

Inclusion criteria:

1. Healthy normotensive pregnant women in their 3rd trimester.
2. Mild PE and severe PE women in their 3rd trimester.

Exclusion criteria:

1. H/O Diabetes, renal disease, chronic hypertension, any thyroid disease, dyslipidemia, bad obstetric history and PE.
2. H/O any chronic inflammatory disease, systemic lupus erythematosus and cardiovascular disease.
3. H/O any metabolic disorder before or during pregnancy.
4. H/O any medication that might affect thyroid function.
5. H/O any acute illness or any addiction.
6. Cases in study group which are in labour or having multiple pregnancy.

Study was approved by ethical committee of the institute. A valid written consent was taken from patients after explaining study to them. Out of 120 subjects, 80 were the cases of newly diagnosed PE patient and 40 were normal pregnant women. Cases were subdivided into separate groups comprising of 40 cases of mild PE and 40 cases of severe PE. This classification of PE patient based upon guidelines given by National High Blood Pressure Education Programme (NHBPEP) working group on high blood pressure in pregnancy.[6] The study groups are shown below:

Group I: 40 Healthy normotensive pregnant women as a control.
Group II: 40 cases of mild PE .
Group III: 40 cases of severe PE.

All cases and controls were evenly matched for parity and maternal age. Participants were selected on the basis of detailed history, clinical examination and laboratory investigations. While recording Blood pressure either in left lateral or sitting position of the right arm roughly horizontal position at heart level. Detailed history of participants including age, sex, history of any medications, addictions and complete obstetric history was taken. Birth weight of babies recorded.

After written informed consent, 12 hour fasting venous blood samples were collected from all pregnant women at least 6 hr before delivery. In preeclamptic group, blood sample is collected when patient presented for evaluation before initiation of medical therapy in plain bulbs. Serum was separated after 1 hour by centrifugation at 3000 rpm for 10 minutes and was tested for Thyroid function tests fT3 , fT4, TSH

Estimation Of fT3, fT4 And TSH

Method: Chemiluminescence assay

Principle: Competitive Chemiluminescence Immunoassay Analog method for free T3.

The essential reagents required for a solid phase enzyme immunoassay include immobilized T3 antibody, enzyme T3 conjugate and native free T3 antigen. The enzyme T3 conjugate should have no measurable binding to serum proteins especially TBG and albumin. The method achieves this goal.

Upon mixing immobilized antibody, enzyme T3 conjugate and a serum containing the native free T3 antigen, a competition reaction results between the native free T3 and the enzyme T3 conjugate for a limited number of insolubulized binding sites. The interaction is illustrated by the followed equation:

$$\mathbf{EnzAg + Ag + Abc.w.} \underset{\mathbf{K_a}}{\rightleftharpoons} \mathbf{AgAbc.w + EnzAg Abc.w.}$$

Abc.w. = Specific Immobilized Antibody (Constant Quantity)
Ag = Native Antigen (Variable Quantity)
EnzAg = Enzyme Antigen Conjugate (Constant Quantity)
AgAbcw. = Antigen- Antibody Complex
EnzAgAbcw. = Enzyme-Antigen Conjugate Antibody Complex
$\mathbf{k_a}$ = Rate Constant of Association
$\mathbf{k_{\_a}}$ = Rate Constant of Disassociation
K = ka / $k_{\_a}$ = Equilibrium Constant

After equilibrium is attained, the antibody-bound fraction is separated from unbound antigen by decantation or aspiration. The enzyme activity, determined by the reaction with substrate that generate light, in the antibody bound fraction is inversely proportional to the native free antigen concentration. By utilizing several different serum

references of known antigen concentration, a dose response curve can be generated from which the antigen concentration of an unknown can be ascertained.

REAGENTS:

A. Human serum Reference – 1 ml/vial

Six vials of serum reference for free tri-iodothyronine of known concentrations in pg/ml. Store at 2 - 8 ºC. A preservative has been added.

For SI units: 1 pg/ml x 1.536 = pmol/L

B. Free T3 Tracer Reagent – 13ml/vial

One vial of tri-iodothyronine horseradish peroxidase (HRP) conjugate in a bovine albumin-stabilizing matrix. A preservative has been added and stored at 2 - 8 ºC.

C. Light Reaction Wells – 96 wells

One 96-well, white micro-plate coated with sheep anti-tri-iodothyronine serum and packed in an aluminium bag with a drying agent. Stored at 2 - 8 ºC.

D. Wash Solution Concentrate – 20 ml

One vial containing a surfactant in buffered saline. A preservative has been added. Stored at 2- 30 ºC.

E. Signal Reagent A – 7 ml/vial

One bottle containing luminal in buffer Stored at 2 – 8 ºC.

F. Signal Reagent B – 7 ml/vial

One bottle containing hydrogen peroxide in buffer Stored at 2 - 8 ºC.

REAGENT PREPARATIONS:

1. Wash Buffer

Dilute contents of Wash concentrate to 1000 ml with distilled or deionised water in a suitable storage container. Store diluted buffer at room temperature 20 - 27 ºC.

2. Working Signal Reagent Solution. Stored at 2 - 8 ºC.

Determine the amount of reagent needed and prepare by mixing equal proportions of Signal Reagent A and Signal Reagent B in a clean, dry container.

PROCEDURE:

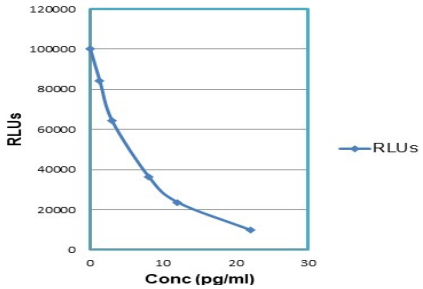
Before proceeding with the assay, bring all reagents, references and controls to room temperature (20 - 27 º C).

1. Format the micro-plate wells for each serum reference, control and patient specimen to be assayed in duplicate. Replace any unused micro-well strips back into the aluminium bag, seal and store at 2 - 8 ºC.
2. Pipette 0.050 ml (50µl) of the appropriate serum reference, control or specimen into the assigned well.
3. Add 0.100 ml (100µl) free T3 –Tracer Reagent to all wells.
4. Swirl the micro-plate gently for 20-30 seconds to mix and cover.
5. Incubate for 45 minutes at room temperature.
6. Discard the content of the micro-plate by decantation or aspiration. If decanting, blot the plate dry with absorbent paper.
7. Add 350µl of wash buffer, decant (tap and blot) or aspirate. Repeat four (4) additional times for a total of five (5) washes.
8. Add 0.100 ml (100µl) of working signal reagent to all wells. Always add reagents in the same order to minimize reaction time difference between wells.
9. Incubate for five (5) minutes in dark.
10. Read the relative light units in each well for 0.2 – 1.0 seconds. The result should be read in thirty (30) minutes of adding substrate solution.

Procedure is same for estimation of serum freeT4 and TSH, with respective reagents and monoclonal antibodies.

Calibration of fT3

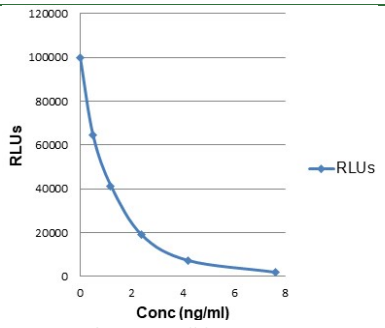
fT3	Conc of calibrators (pg/ml)	RLUs
A	0	100000
B	1.3	84180
C	3.0	64281
D	8.0	36489
E	12.0	23624
F	22.0	9846



Graph 1: FT3 callibration curve

Calibration of fT4

fT4 calibrators	Conc of calibrators (ng/dl)	RLUs
A	0	100000
B	0.5	64509
C	1.2	41295
D	2.4	18866
E	4.2	7296
F	7.6	1888



Graph 2: FT4 cllibration curve

Principle for estimation of TSH: immunoenzymometric assay

This requires high affinity and specific antibodies (enzyme conjugated and immobilized) with different and distinct epitope recognition, in excess and native antigen. In this procedure, the immobilization takes place at the surface of an opaque chemiluminescent reaction cell through the interaction of streptavidin coated on the opaque reaction cell and exogenously added biotinylated monoclonal antibody coupled to the analyte of interest. Upon mixing monoclonal biotinylated antibody and test serum containing the native antigen, reaction results between native antigen and antibodies to form a soluble sandwich complex.

The interaction is illustrated as follows:

$$\mathbf{Enz_{Ab(p)} + Ag_{(TSH)} + Bio_{Ab(m)} \underset{k_b}{\overset{k_a}{\rightleftharpoons}} Enz_{Ab}\text{-}Ag_{(TSH)}\text{-}Bio_{Ab(m)}}$$

$Enz_{Ab(p)}$ = enzyme labelled polyclonal antibody (excess quantity)

$Ag_{(TSH)}$ = native antigen (variable quantity)

$Bio_{Ab(m)}$ = biotinylated monoclonal antibody (excess quantity)

Enz_{Ab}- $Ag_{(TSH)}$ -$Bio_{Ab(m)}$ = antigen antibody sandwich complex

k_a = rate constant of association

k_b = rate constant of dissociation

Simultaneously, the complex is deposited in reaction well through the high affinity reaction of strepavidin and biotinylated antibody. The reaction as follows:

Enz_{Ab}- $Ag_{(TSH)}$ -$Bio_{Ab(m)}$ + streptavidin$_{cw}$ immobilized complex ⟶

streptavidin$_{cw}$ = streptavidin immobilized on well

Immobilized complex = sandwich complex bound to solid surface.

After equilibrium is attained, the antibody bound fraction is separated from unbound antigen by decantation. The enzyme activity, determined by the reaction with the substrate that generates light, in the antibody bound fraction is directly proportional to the native antigen concentration.

Reference Values: provided by MONOBIND, INC. Lake forest, (USA)

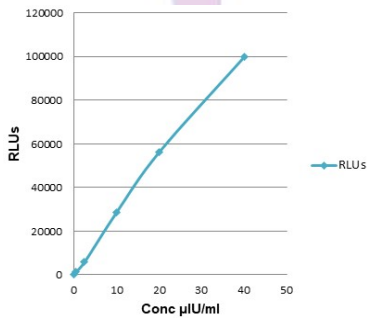
Free T3: 1.5 – 4.2 pg/ml

Free T4: 0.7 – 1.8 ng/ml

TSH: 0.3 – 5.00 µIU/ml

Calibration of TSH

TSH calibrators	Conc. of calibrator (µIU/ml)	RLUs
A	0	166
B	0.5	1253
C	2.5	5860
D	10.0	28598
E	20.0	56238
F	40.0	100000



Graph 3: TSH Callibration curve

RESULTS

The mean values of maternal age in all three are not statistically significant. Mean values Group I: 23.73 ± 2.58, Group II: 23.25 ± 2.79, Group III: 22.45 ± 2.31). Mean gestational age at the time of serum sampling in normal pregnant women is 36.15 ± 1.42 and it decreases in mild (34.33 ± 2.46) and severe PE (33.10 ± 1.68) having highly significant P value. (table 1) While SBP and DBP increases with severity of PE as compared to normal pregnant women having highly significant P value (<0.0001). As blood pressure is indicator for the severity of PE because more is SBP and DBP more severe is the PE. (table 1) Urine protein is nil in group I and it increases with severity of PE. Proteinuria and blood pressure are used as parameters for severity of PE. The mean value of birth weight is normal in healthy pregnant women 2.89 ± 0.17 but it decreases in mild PE (2.54 ± 0.08) to more decrease in severe PE (2.35 ± 0.08) having highly significant p value <0.0001.

(table 1) In our study, the mean level of TSH within normal level in normal pregnant women is 2.32 ± 0.58. While in mild PE is 3.99 ± 0.67 and in severe PE is 5.66 ± 1.00 with highly significant P value<0.0001. (table 2) In our study, fT3 level is significantly higher (P <0.0001) in normal pregnant women (3.41 ± 0.37) than PE women and it significantly decreases (p <0.0001) with severity of PE with mean level in mild PE is 3.06 ± 0.33 and in severe PE is 2.77 ± 0.43. Mean fT4 level is not statistically significant among three groups (mean level normal pregnant: 2.23 ± 0.40, mild PE: 2.26 ± 0.23 and severe PE: 2.34 ± 0.29). (table 2) In our study, TSH is correlated positively with systolic B.P. in both mild PE and severe PE(r=0.53, r=0.37).It is also correlated positively with diastolic B.P. in both mild and severe PE (r=0.51, r=0.35). TSH is correlated negatively with birth weight in both mild and severe PE(r=-0.44, r=-0.41). (table 3,4) TSH is also correlated positively with blood pressure (both systolic and diastolic) in both groups of mild PE and severe PE (r=0.5 and r=0.3) and correlated negatively with birth weight(r = -0.44,r= -0.41). (table 3,4)

Table 1: Demographic parameters in studied groups

Parameters	Group I (control) n=40 n=40	Group II (mild PE) n=40 n=40	Group III (severe PE) n=40	P value
Maternal age(yrs)	23.73 ± 2.58	23.25 ± 2.79	22.45± 2.31	0.13
Gest age at serum sampling (wks)	36.15 ± 1.42	34.33 ± 2.46	33.10± 1.68	**0.01**
Systolic BP (mm of Hg)	117.55±5.21	150.65±4.54	168.6± 4.08	**<0.0001***
Diastolic BP (mm of Hg)	78 ± 4.75	98.85 ± 3.48	118.5± 3.67	**<0.0001***
Urine protein	Nil	1+	2+	
Birth weight (kg)	2.89 ± 0.17	2.54 ± 0.08	2.35 ± 0.08	**<0.0001***

Comparison between women with mild and severe = p value

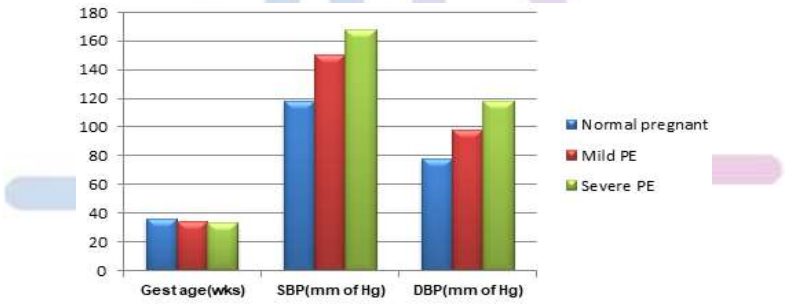


Figure 1: Demographic parameters in studied groups

Table 2: Thyroid Function Tests in studied groups

Parameter	Group I (control) n=40 n=40 n=40	Group II (mildPE) n=40	Group III (severePE) n=40n=40	P
TSH(µIU/ml) (0.3-5.0)	2.32 ± 0.58	3.99± 0.67	5.66 ± 1.00	**< 0.0001***
fT3(pg/ml) (1.5-4.2)	3.41 ± 0.37	3.06± 0.33	2.77 ± 0.43	**0.001**
fT4(ng/ml) (0.7-1.8)	2.23 ± 0.40	2.26± 0.23	2.34 ± 0.29	0.17

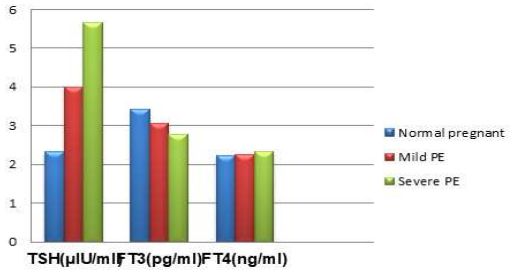


Figure 2: Thyroid Function Tests in studied groups

Table 3: Correlation coefficient(r value) in group II (Mild PE)

Parameters	r value	P value
TSH vs SBP	0.53	< 0.000
TSH vs DBP	0.51	0.000
TSH vs Birth wt	-0.44	0.004

Correlation coefficient(**r value**) **0.3-0.5** is small correlation. **0.5-0.7** is large correlation. **1** is perfect correlation.

Table 4: Correlation coefficient(r value) in group III (severe PE)

Parameters	r value	P value
TSH vs SBP	0.37	0.02
TSH vs DBP	0.35	0.03
TSH vs Birth wt	-0.41	0.01

DISCUSSION

In our study, the mean level of TSH within normal level in normal pregnant women is 2.32 + 0.58. While in mild PE is 3.99 + 0.67 and in severe PE is 5.66 + 1.00 with highly significant P value<0.0001. Ashok Kumar and his co-worker (2005): In their study the mean fT3 and fT4 titers were not significantly different in the two groups (fT3: *P* = 0.24; fT4: *P* = 0.25). The mean TSH value was significantly higher in the preeclamptic women than that of controls (*P* < 0.001). [7]

Dhananjaya BS and his associate (2012) In their study found that Thyroid profile values (T3 and T4) in normal and pre-eclampsia groups were within normal limits. Patients with pre-eclampsia showed significantly increased TSH levels (p< 0.042) compared to normal. [8] In our study, fT3 level is significantly higher (P <0.0001) in normal pregnant women (3.41 + 0.37) than PE women and it significantly decreases (p <0.0001) with severity of PE with mean level in mild PE is 3.06 + 0.33 and in severe PE is 2.77 + 0.43. Mean fT4 level is not statistically significant among three groups (mean level normal pregnant: 2.23 + 0.40, mild PE: 2.26 + 0.23 and severe PE: 2.34 + 0.29). These findings in our study correlate with M Hafizur Rahman *et al.* (20007) where they studied Serum Thyroxine and Triiodothyronine Levels in Normal Pregnancy and Pre-Eclampsia. They found n pre-eclampsia mean serum total and free T4 were non-significantly higher when total and free T3 were significantly lower than that of normal pregnancy.[9] Similar to our study ,Palanisamy Pasupathi *et al.* (2009) observed The mean TSH level for PE woman was even higher than in either other the other two groups and the mean TSH level in PE were significantly higher than that in normal pregnant women (*p* < 0.001). However, fT4 levels did not significantly differ between women with normal pregnancies and those with PE. Subjects with PE had significantly higher fT3 than non-pregnant women but a significantly lower mean level than women with normal pregnancies. [10]

Asmehan A. Al-Naqeeb *et al.*(2010) showed A significant increase in the level of TSH in mild preeclamptic women as compared to control (p<0.05) and severe PE (p<0.01) as compared to control too. T3 level was higher in mild PE (p<0.05) and severe (p<0.01) as compared to normotensive pregnant, but T4 does not have significant changes in preeclamptic groups as compared to control. [11] In our study, TSH is correlated positively with systolic B.P. in both mild PE and severe PE(r=0.53, r=0.37).It is also correlated positively with diastolic B.P. in both mild and severe PE (r=0.51, r=0.35). TSH is correlated negatively with birth weight in both mild and severe PE(r=-0.44, r=-0.41). This finding of negative correlation of TSH with birth weight in our study correlate with following study: Divya Sardana *et al.* (2009) found A significant negative correlation was observed between birth weight and TSH levels in preeclamptic women (r=-0.296, p<0.001). There is a state of hyperthyroxinemia in normal pregnancy and in PE, a biochemical hypothyroidism (raised TSH) occurs. Thyroid hormonal levels correlated with the severity and outcome of PE[6].

The possible mechanism of thyroid dysfunction in normal pregnant women and PE:

1. **Changes in Thyroid Function Tests in normal pregnant women:**

In pregnancy serum TT4 and TT3 was higher, while fT4 and fT3 was similar when compared to non-pregnant women. Increase in TT4 and TT3 is due to in circulating TBG (major T4 binding protein), which is induced by high estrogen level. Along with that placental production of serum HCG, mental stress in pregnancy and increased metabolic demand have important role for elevate thyroid hormonal level in pregnancy. During pregnancy, estrogen stimulates the liver to increase the production of protein leading to more TBG production. Increased estrogen reduces peripheral degradation by oligosaccharide modification. Increased TBG in serum leading to more hormones bind to TBG so that thyroid hormone levels increases but free form remains unchanged. There is controversy in different studies

regarding free thyroid hormone level in normal pregnancy which may remain normal, increases or decreases compared to non-pregnant women[9].

2. Mechanism of Thyroid function tests alteration in PE:

1. The mechanism of thyroid hormone alteration in preeclamptic women is not well known. Mild changes in thyroid hormone may occur due to non-thyroidal illness as a stress factor as well as it may be due to decreased plasma albumin concentration. Due to loss of protein serum TT4 and TT3 were decreased and TSH was increased in preeclamptic women in their 3rd trimester. As compared to normal pregnant women higher fT4 and TT4 along with lower fT3 and TT3 were observed in preeclamptic women. Free thyroid hormones are not related to plasma albumin level but fT3 levels are related to decreased plasma albumin level while fT4 is not related to plasma albumin. Hence, tt has been suggested that reduced serum concentrations of thyroid hormones may be due to loss of protein and protein bound hormones in urine[7].
2. PE is pregnancy induced autointoxication with multisystem disorder with involvement of brain, liver and kidneys. Functional disorder in these organs is observed in PE. On the other hand liver and kidney are the important organ in peripheral deiodination (conversion of T4 to T3) and maintenance of normal blood levels of T4 and T3, so that involvement of liver and kidney is likely to change serum T4 and T3 levels in PE[9].
3. Increase in TSH levels and moderate decrease in thyroid hormone in maternal serum is correlated with severity of PE. Reduced serum concentrations of TBG, T3 and T4 may also be explained by the faulty estrogen production due to placental dysfunction in preeclamptic women[7].

CONCLUSION

Evaluating thyroid screening during pregnancy might be of help in preventing the occurrence of low birth weight and instituting timely intervention and appropriate measures in terms of possible thyroid hormone administration in preterm infants in future.

REFERENCES

1. Tavana Z, Zolghadri J, Madadi G. The Relationship Between Maternal Serum Highly Sensitive C-Reactive Protein, Leptin And Hypertensive Disorders Of Pregnancy. The Internet Journal of Endocrinology. 2011;6(2).
2. Prakash J, Pandey LK, Singh AK, Kar B. Hypertension in Pregnancy: Hospital Based Study. JAPI. 2006 April; 54:273-278.
3. Sachdeva PD, Patel BG, Bhatt MV. A study of incidence and management of PIH in central Gujarat, India. Ijupls. 2011 Nov-Dec; 1(3):61-70.
4. Diagnosis and management of PE and eclampsia. ACOG Practice Bulletin no.33.Clinical management guidelines for obstetrician-gynecologist. 2002 Jan; 33:159-167.
5. Wagner LK. Diagnosis and Management of PE. Am Fam Physician.2004 Dec15; 70(12):2317-24.
6. Sardana D, Nanda S, Kharb S. Thyroid hormones in pregnancy and PE. J Turkish-German Gynecol Assoc. 2009;10:168-71.
7. Kumar A, Ghosh BK,Murthy NS. Maternal thyroid hormonal status in PE. Indian J Med Sci 2005; 59: 57-63.
8. Dhananjaya BS, Sendil KD, Venkatesh G, Murthy N, Shashiraj HK. TSH level as a possible indicator of pre-eclampsia. Journal of Clinical and Diagnostic Research [serial online] 2011 Dec [cited: 2012 Oct 2]; 5: 1542-1543.
9. Rahman MH, Chowdhury MA, Alam MT. Serum thyroxine and triiodothyronine levels in normal pregnancy and pre-eclampsia. The Journal of Teachers Association RMC, Rajshahi TAJ. 2007 June; 20(1); 06-10.
10. Pasupathi P, Mathiyalagan D, Rani P, Vidhya Sankar KB, and Satish kumar SP. Evaluation of serum lipids and thyroid hormone changes in non-pregnant, pregnant and PE women. Thyroid Science. 2009;4(10):CLS1-6.
11. Al-Naqeeb AA. Correlation between thyroid-related hormones and PE. Iraqi Sci. J. Nursing. 2010; 23.

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