

A COMPARATIVE STUDY OF THYROID HORMONE LEVELS IN PREECLAMPTIC WOMEN AND NORMAL PREGNANT WOMEN

¹Iqbal Ahmed, ¹Jhansi Rani C, ¹Bhanuja Rani, ²Sarojini, ¹Hemamalini

Department of Biochemistry, GMC, Secunderabasd. T.S.
Specialist Doctor, Dept. of General Medicine, APVVP, A.P.

Corresponding Author

Dr. B. Bhanuja Rani
Assistant Professor,
Biochemistry Department
Gandhi Medical College, Secunderabad.

ABSTRACT

Introduction: Preeclampsia is a common complication of pregnancy associated with increased morbidity and mortality in mother and fetus. During pregnancy there is an increased demand and synthesis of thyroid hormones. Thyroid Hormones plays a role in Placental development and is an important regulator of various metabolic and Inflammatory process.

Aim: To compare the thyroid hormone level in severe, moderate, mild preeclamptic woman with normal pregnant woman.

Materials and methods: A total of 60 subjects aged 25-40 years were selected from Antenatal clinic, Department of obstetrics and Gynecology, Gandhi Hospital, Secunderabad. Thyroid profile was analyzed by chemiluminiscence immunoassay.

Results: The mean and S.D of serum TSH in cases is 5.6 ± 4.4 as compared to 3.7 ± 1.9 in controls p value 0.008 and pearson correlation 0.33 which is considered highly significant. The mean and S.D of serum T₃ in controls is 1.77 ± 0.64 as compared to 1.65 ± 0.6 in cases. The mean and S. D of serum T₄ in controls is 9.5 ± 2.7 as compared to 11.6 ± 4.06 .

Conclusion: Screening of thyroid profile should be done in all pregnant women to identify thyroid abnormalities and to prevent severity of morbidity and mortality associating with preeclampsia.

Keywords: Thyroid disorders, Hypothyroidism, T₃, T₄ and TSH.

INTRODUCTION

Thyroid dysfunction is a disorders of the thyroid gland manifests as hyperthyroidism or hypothyroidism which reflects in the levels of Thyroid Stimulating Hormone (TSH) (1). During pregnancy, there is an increased thyroid demand leading to increased iodine uptake and synthesis of thyroid hormones. Estrogen induces a rise in serum TBG and the placenta releases several thyroid stimulatory factors in excess like β hCG. Alpha subunit of β hCG is identical to that of TSH and has weak thyrotropic activity (2).

Hypothyroidism has been listed as one of the causes of high blood pressure (3). In preeclampsia, there is failure of estrogen production due to placental dysfunction resulting in lowering of TBG, TT₃, TT₄ along with growth retardation of the fetus (4). Increasing evidence suggests that oxidative stress and altered endothelial cell function may have a role in preeclampsia (5-7). Also, oxidative stress has been proposed as another contributing source of the hyperuricemia noted in preeclampsia apart from renal dysfunction (9). In preeclampsia, an increase in the superoxide anion, which may inactivate NO, leading to reduced relaxation and increased vasoconstriction (7,8). Experimental studies have indicated that release of NO is altered in hypothyroidism and the resulting endothelial cell dysfunction might be a pathogenetic mechanism for hypothyroidism in preeclampsia (10).

In preeclampsia there is loss of proteins and protein-bound hormones in the urine leading to low TT₃ levels (11). Decreased peripheral conversion of T₄ to T₃ causes decrease in the T₃ levels due to involvement of the liver and kidney leads to "low T₃ syndrome". (12-14).

The aim of the study was to evaluate the thyroid hormone levels in Pre-eclampsia in South Indian Subjects.

Materials and methods

Subjects

The present study was carried out in the Department of Bio-chemistry Gandhi Medical College, Secunderabad. The cases were selected from those attended, Antenatal clinic, Department of obstetrics and Gynecology, Gandhi Hospital, Secunderabad. The Investigations were carried out in Bio-Chemistry laboratory, Gandhi Medical College, Secunderabad.

Design

The total number of subjects included in the study was 60 and divided into two groups. Group I consists of 30 patients with pre-eclampsia as cases, while Group-II consists of 30 healthy pregnant of age matched as controls. This is a case control study.

Criteria for Selection

All cases of preeclamptic patients, age matched healthy pregnant as controls attending OBG department are included in the study. Pregnant patient with eclampsia, Anemia, Diabetes mellitus, Essential hypertension, Renal insufficiency, cardiovascular disease, Hypothyroidism and those who are on Systemic drug therapy such as thyroxin, antithyroid drugs, glucocorticoids are excluded from the study.

Blood Sample Collection

5ml venous blood sample was obtained from every volunteer into plain tubes (BD vacutainer system). All the blood samples were immediately carried to the Biochemistry Laboratory and centrifuged at 3000rpm for 10 minutes. Urine sample also collected in sterile container and centrifuged.

The following parameters are analyzed:

Thyroid profile - CLIA by Siemens Advia Centaur fully automated (T₃, T₄ and TSH) immuno analyzer machine

Renal profile -Beckman Coulter analyzer AU 5800. (Blood urea, serum Uric acid)

Total Proteins, Serum Albumin - Beckman Coulter AU 5800

Ethics approval

The study protocol was reviewed and approved by the Institutional Ethics committee, at Gandhi Medical College, Secunderabad, 2019, and written informed consent form was obtained from all participants.

RESULTS

The total number of subjects included in the study was 60 and divided into two groups. Group I consists 30 patients with pre-eclampsia as cases, while Group-II consists consists of 30 healthy pregnant of age matched as controls. The mean and S.D of serum TSH in cases is 5.6 ± 4.4 as compared to 3.7 ± 1.9 in controls p value 0.008 and Pearson correlation 0.33 which is considered highly significant. [Table 1] The mean and S.D of serum T₃ in controls is 1.77 ± 0.64 as compared to 1.65 ± 0.6 in cases p value 0.01 and Pearson correlation 0.9 which is considered highly significant. The mean and S. D of serum T₄ in controls is 9.5 ± 2.7 as compared to 11.6 ± 4.06 p value 0.02 and Pearson correlation 0.4 which is considered highly significant. The mean and S.D of serum Total proteins in controls is 6.2 ± 0.6 as compared to 5.6 ± 0.6 in cases. The mean and S.D of serum Sr Albumin in controls is 3 ± 0.4 as compared to 2.9 ± 0.3 in cases. There is no significant variation in the levels of the mean and S.D of Hb, Total Bilirubin, Sr Creatinine, Bl Urea, Uric Acid in controls as compared in cases. (Table-2, Fig 1&2).

Table 1: Comparisons of T3, T4, TSH in Pre eclampsia and Normal Pregnant Women

		T3	T4	TSH
NORMAL PREGNANT WOMEN	MEAN	1.77	9.5	3.7
	S D	0.64	2.7	1.9
PRE-ECLAMPSIA	MEAN	1.65	11.6	5.6
	S D	0.6	4.06	4.4
P Value		0.01	0.002	0.008
Pearson Correlation		0.9	0.4	0.33

Table 2: Comparisons of Hb, Total Protein, Sr Albumin, T Bilirubin, Sr Creatinine, BI Urea, UA in Preeclampsia and Normal Pregnant Women

		Hb	T Protein	Sr Albumin	T bilirubin	Sr Creatinine	BI Urea	UA
NORMAL PREGNANT WOMEN	MEAN	11.1	6.2	3	0.5	0.68	25.2	4.6
	SD	1.1	0.6	0.4	0.2	0.2	12.6	0.89
PRE-ECLAMPSIA	MEAN	9.5	5.6	2.9	0.6	0.7	23.6	5.9
	SD	1	0.6	0.3	0.19	0.4	12.9	1.9

Figure 1: Comparisons of FBS, T3, T4, TSH, Hb, Total Protein, Sr Albumin, T Bilirubin, Sr Creatinine, BI Urea, UA in Preeclampsia and Normal Pregnant Women

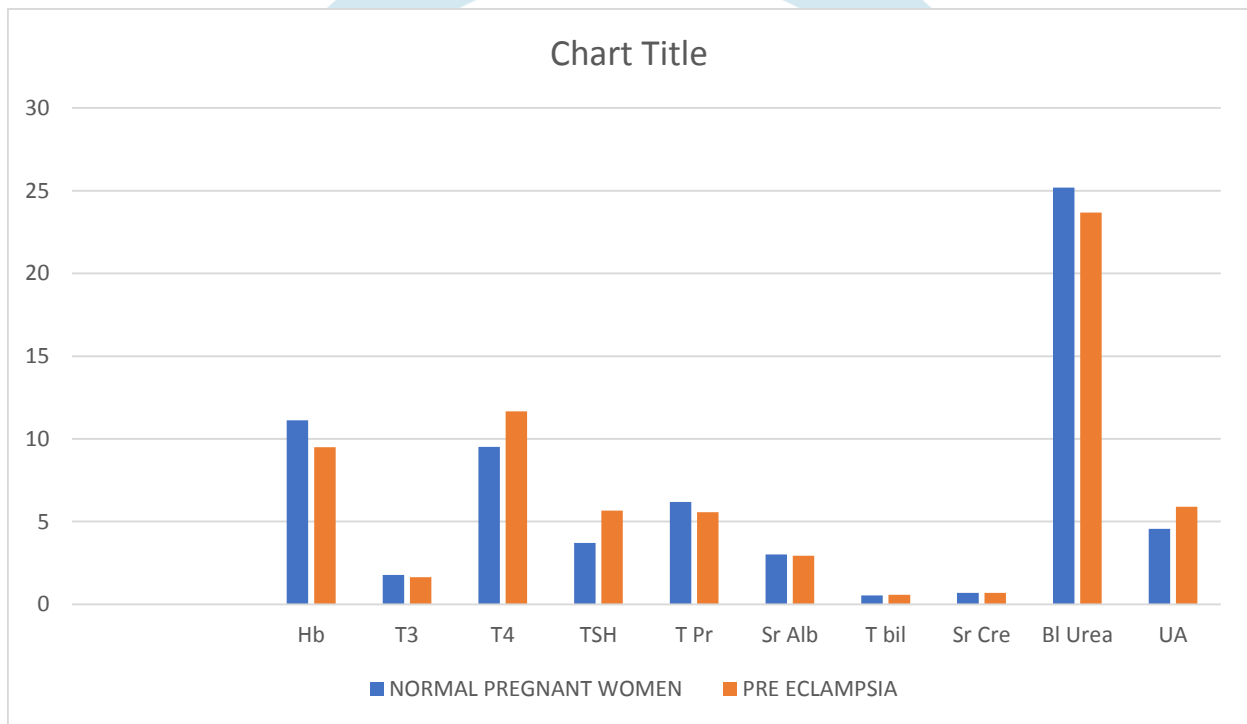
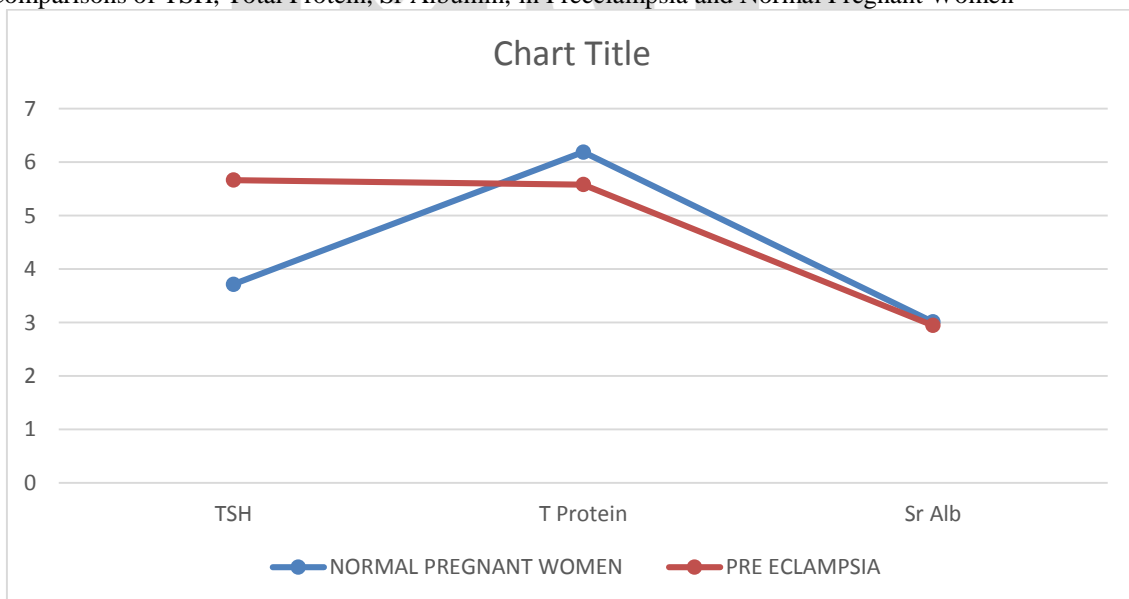


Figure 2: Comparisons of TSH, Total Protein, Sr Albumin, in Preeclampsia and Normal Pregnant Women



DISCUSSION:

Preeclampsia is a major public health problem due to its frequency as well as its related maternal and perinatal morbidity and mortality, with a prevalence of 4.6% among pregnant women worldwide [15]. It is not only associated with adverse pregnant outcomes, but also contribute to higher risk of cardiovascular diseases, renal failure, type 2 diabetes mellitus, hypothyroidism and cognitive defects in future [16]. Furthermore, children born from preeclamptic pregnancies are more prone to hypertension, insulin resistance and diabetes mellitus, neurological complications, stroke, and mental disorders in their later lives [16].

Thyroid dysfunction is common among pregnant women. In the present study the levels of TSH in the preeclamptic pregnancies is higher 5.6 ± 4.4 as compared to 3.7 ± 1.9 in normal pregnancies with p value 0.008 and Pearson correlation 0.33 which is considered highly significant, which is correlated with the study of Divya sardana Smitha nanda et al. With due regard to the negative impacts of preeclampsia on pregnancy, any change may be important. Damage of endothelial cells and vasospasm are major pathologies during preeclampsia and eclampsia. Human gestation is dependent upon at least three temporally different vascular processes: (a) adequate uterine angiogenesis at the time of implantation, (b) development and expansion of the placental-villous-vasculature soon after implantation and (c) remodeling of the maternal uterine circulation near the maternal-fetal interface (17).

Consequently, it is possible that the disruption of these early vascular events may contribute to the pathology of conditions like preeclampsia or intra uterine growth retardation of the fetus. Endothelial activation/dysfunction is a central pathogenic feature in women with preeclampsia, which is a multiple system disorder during human pregnancy (18-19). Increased circulating VEGF-1 concentration in preeclamptic women were associated with decreased circulating levels of free VEGF and PlGF, leading to an anti-angiogenic state and causing endothelial cell dysfunction (20-22).

There is strong evidence that TSH can act as a tissue specific angiogenesis in physiological and pathological conditions. Thus, increased levels of VEGF and TSH protein correlated with each other. TSH up regulates VEGF expression in vivo and vitro (23).

Khadem study does not support the hypothesis that changes TSH levels could be a possible etiology of preeclampsia (24), which is not correlated with the present study. Thyroid dysfunction can be associated with proteinuria, which is known [25] to result in increased excretion of thyroxine and thyroid-binding globulins. Rare cases, have been reported [26,27] where proteinuria is severe enough to result in losses of thyroid-binding globulins and thyroxine that cannot be compensated by the body.

It can be suggested that women who develop preeclampsia are more likely to have lower normal limits of thyroid function. Study of maternal thyroid function and detection of lower normal limits in pregnant women may concern us about development of preeclampsia.

CONCLUSION:

Hypothyroidism may be a modifiable risk factor for preeclampsia. Thyroid screening early in pregnancy may be helpful in predicting the occurrence of preeclampsia and timely thyroid hormone administration can reduce the maternal and perinatal morbidity and mortality associated with preeclampsia. Failure to recognize the presence of abnormal thyroid function may be a primary cause of poor management of Pre-eclampsia.

ACKNOWLEDGEMENTS

I am grateful to my parents for rendering their moral support and co-operation during my study and in the preparation of the Original Article. I thank all the staff members of the department and 24 hrs Biochemistry labs, Gandhi Medical College, Secunderabad their co-operation during my study.

CONFLICT OF INTEREST: Nil.

FUNDING: None.

REFERENCES

1. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, Evans JG, Young E, Bird T, Smith PA. The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol (Oxf)*. 1977 Dec;7(6):481-93.
2. Brent GA. Maternal thyroid function: interpretation of thyroid function tests in pregnancy. *Clin Obstet Gynecology*. 1997;40:3-15.
3. Endo T, Komiya I, Tsukui T. Reevaluation of a possible high incidence of hypertensive in hypothyroid patients. *Am Heart J*. 1979;98:684-8
4. Kaye E, Sahin Y, Ozkececi Z, Pasaoglu H. Relation between birth weight and thyroid function in preeclampsia-eclampsia. *Gynecol Obstet invest*. 1994;37:30-3.
5. Kharb S, Gulati N, Singh V, Singh GP. Lipid peroxidation and vitamin E levels in preeclampsia. *Gynecol Obstet Invest*. 1998;46:238-40.
6. Kharb S. Total free radical trapping antioxidant potential in preeclampsia. *Int J Gynecol Obstet*. 2000;69:23-6.
7. Kumar CA, Das UN. Lipid peroxides, anti-oxidants and nitric oxide in patients with preeclampsia and essential hypertension. *Med Sci Monitor*. 2000;6:901-7.

8. Kharb S, Gulati N, Singh V, Singh GP. Superoxide formation and glutathione levels in patients with preeclampsia. *Gynecol Obstet Invest.* 2000;49:28–30.
9. Kharb S, Singh GP. Hyperuricemia, Oxidative stress in preeclampsia. *Clin Chim Acta.* 2001;305:201–3.
10. Kumar A, Ghosh BK, Murthy NS. Maternal thyroid hormonal status in preeclampsia. *Indian J Med Sci.* 2005;59:57–63.
11. Osathanondh R, Tulchinsky D, Chopra IJ. Total and free thyroxine and triiodothyronine in normal and complicated pregnancy. *J Clin Endocrinol Metab.* 1976;42:98–104.
12. Skjoldebrand L, Brundin J, Carlstrom A, et al. Thyroxine-binding globulin spontaneous abortion. *Gynecol Obstet Invest.* 1986;21:187–92.
13. Basbug M, Aygen E, Tayyar M, Tutus A, Kaya E, Oktem O. Correlation between maternal thyroid function tests and endothelin in preeclampsia – eclampsia. *Obstet Gynecol.* 1999;94:551–5.
14. Tolino A, De Concilio B, Montemagno U. Thyroid hormones in human pregnancy. *Acta Obstet Gynecol Scand.* 1985;64:557–9.
15. Abalos E, Cuesta C, Grosso AL, Chou D, Say L. Global and regional estimates of preeclampsia and eclampsia: a systematic review. *Eur J Obstet Gynecol Reprod Biol.* 2013;170(1):1–7.
16. Tranquilli AL. Prediction, medical illness and the risk of pre-eclampsia. *Pregnancy Hypertens.* 2014;4(3):245.
17. Torry DS, Hinrichs M, Torry RJ. Determinants of placental vascularity. *Am J Reprod Immunol.* 2004;(51):257–268.
18. Hubel CA, Sibose PI, Crockere IP. Endothelial progenitor cells: Their potential role in pregnancy and preeclampsia. *Pregnancy Hypertension.* 2011;1(1):48–58.
19. Wang Y, Gu Y, Zhang Y, Lewis DF. Evidence of endothelial dysfunction in preeclampsia: decreased endothelial nitric oxide synthase expression is associated with increased cell permeability in endothelial cells from preeclampsia. *Am J Obstet Gynecol.* 2004;190(3):817–824.
20. Polliotti BM, Fry AG, Saller DN, Mooney RA, Cox C, Miller RK. Second-trimester maternal serum placental growth factor and vascular endothelial growth factor for predicting severe, early-onset preeclampsia. *Obstet Gynecol.* 2003;101(6):1266–1274.
21. Koga K, Osuga Y, Yoshino O. et al. Elevated serum soluble vascular endothelial growth factor receptor 1 (sVEGFR-1) levels in women with preeclampsia. *J Clin Endocrinol.* 2003;(88):2348–2351.
22. Tsatsaris V, Goffin F, Munaut C. et al. Over expression of the soluble vascular endothelial growth factor receptor in preeclamptic patients: pathophysiological consequences. *J Clin Endocrinol Metab.* 2003;(88):5555–5563.
23. Reisinger K, Baal N, McKinnon T, Munstedt K, Zygmunt M. The gonadotropins: Tissue-specific angiogenic factors? *Mol Cell Endocrinol.* 2007;269(1-2):65–80.
24. Khadem N, Ayatollahi H, Vahid Roodsari F, Ayati S, Dalili E, Shahabian M. et al. Comparison of serum levels of Triiodothyronine (T3), Thyroxine (T4), and Thyroid- Stimulating Hormone (TSH) in preeclampsia and normal pregnancy. *Iranian Journal of Reproductive Medicine,* 2012;10(1):47–52.
25. Patel S, Robinson S, Bidgood RJ, Edmonds CJ. A pre-eclamptic-like syndrome associated with hypothyroidism during pregnancy. *Quarterly Journal of Medicine.* 1991;79(289):435–441.
26. Gilles R, et al. Thyroid function in patients with proteinuria. *Netherlands Journal of Medicine.* 2008;66(11):483–485.
27. Chandurkar V, Shik J, Randell E. Exacerbation of underlying hypothyroidism caused by proteinuria and induction of urinary thyroxine loss: case report and subsequent investigation. *Endocrine Practice.* 2008;14(1):97–103.

