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Hypothyroidism as a bio marker of preeclampsia: Our experience

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Abstract

Aim: To evaluate maternal thyroid hormonal status in women with and without preeclampsia and to find out association between hypothyroidism and preeclampsia.

Method: In this prospective case control study 40 women diagnosed as preeclampsia were compared with 35 healthy pregnant women. Thyroid function test was done in both groups of women and statistical analysis was done to find out association of thyroid hormones with preeclampsia. Obstetric outcome was analysed.

Result: Mean FT3 and TSH were significantly different in preeclamptic women. FT4 was comparable in both groups. Age, parity and BMI were not influenced by thyroid hormones. No correlation between severity of preeclampsia and thyroid hormonal status was observed. Gestational age at birth was significantly decreased and cesarean rate was significantly high in preeclampsia. Low birth weight was significant in preeclampsia.

Conclusion: Hypothyroidism is not significantly associated with preeclampsia. No correlation between hypothyroidism and severity of preeclampsia is observed.

Keywords: preeclampsia, hypothyroidism, TSH, pregnancy

Introduction

Preeclampsia is a multiorgan disorder characterized by hypertension and proteinuria leading to maternal and perinatal morbidity and mortality [1]. About 5-15% of pregnancies are complicated by preeclampsia. The etiology of preeclampsia is still an enigma. Genetic, environmental, immunological, and endocrinological factors are responsible for the abnormal placentation in preeclampsia [2]. Resulting oxidative stress and endothelial dysfunction play a role in the pathogenesis of preeclampsia. In preeclampsia, there is an increase of superoxide anion which inactivates nitric oxide. This inactivation of nitric oxide leads to vasospasm pathognomonic of preeclampsia [2]. In normal pregnancy thyroid hormone levels are altered to some extent. The thyrotrophic alpha subunit of β HCG and high level of estrogen in normal pregnancy causes significant increase in thyroglobulin, TT4 and TT3 [3]. In preeclampsia, the failure of estrogen production results in lower TGB, TT3, TT4 along with fetal growth restriction [4]. It has been reported that women with subclinical hypothyroidism identified during pregnancy have an increased risk of severe preeclampsia when compared with euthyroid women [5]. The mechanism and clinical significance of hypothyroidism in preeclampsia is controversial and may be related to decreased plasma protein concentration and increased endothelin (potent vasoconstrictor) level [6]. High levels of soluble FMS-like tyrosine kinase 1(SFLT-1) found in preeclampsia blocks the vascular endothelial growth factor (VEGF). Studies report that increased SFLT level, by blocking VEGF is associated with hypothyroidism [7]. This study was conducted to find out the association between hypothyroidism and preeclampsia.

Materials and Methods

Study Design: Prospective case control study done at Institute of Obstetrics & Gynaecology, Chennai from October 2016 to April 2017.

Subjects: 40 pregnant women diagnosed as preeclampsia and 35 healthy pregnant women chosen as controls were included in the study.

Exclusion Criteria: Pregnant women with H/o thyroid disorder, renal disease, chronic hypertension, medication affecting thyroid function and multiple pregnancy were excluded.

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Methods: Pregnant women with blood pressure more than 140/90 mm Hg with proteinuria (more than 300 mg/l in 24 hrs urine) on 2 or more occasions atleast 6 hrs apart, after 20 weeks of gestation were diagnosed as preeclampsia. Healthy normotensive pregnant women admitted in labour room were selected as control for this study. After getting informed consent, data regarding name, age, symptoms, parity, height and weight were recorded. 10 ml of venous blood was drawn and serum was used for thyroid hormone analysis (FT3, FT4 and TSH) using chemiluminescent assay. The normal value for TSH in our study is 0.3 - 3 mIU/l. Statistical analysis was done using t-Test for comparing means and Pearson chi square test for comparing categorical parameters. P value less than 0.05 was considered as significant.

Table 1: Distribution of thyroid hormone

	Preeclampsia	control	t - Test	P value
Mean FT3 pg/ml	1.37 ± 0.50	1.83 ± 0.42	-4.28	0.0001
Mean FT4 µg/dl	8.08 ± 3.19	9.18 ± 2.30	-1.69	0.09
Mean TSH mIU/l	4.10 ± 3.79	2.69 ± 1.32	2.09	0.04

Table 2: Distribution according to thyroid status

	Preeclampsia (n=40)	Control (n=35)
Hypothyroid	23 (57.5%)	15 (43%)
Euthyroid	17 (42.5%)	20 (57%)

p value =0.20

Table 3: Distribution according to age

Age (years)	Preeclampsia (n=40)		Control (n=35)
	Euthyroid	Hypothyroid	
< 20	0 (0%)	2 (5%)	1 (2.9%)
21-25	10 (25%)	12 (30%)	16 (45.7%)
26-30	4 (10%)	8 (20%)	17 (48.5%)
31-35	3 (7.5%)	1 (2.5%)	1 (2.9%)

p value = 0.30 (comparing preeclampsia with control)

p value = 0.50 (comparing Euthyroid and Hypothyroid preeclamptic women)

Table 4: Distribution according to parity

Parity	Preeclampsia (n=40)		Control (n=35)
	Euthyroid	Hypothyroid	
primi	11 (27.5%)	9 (22.5%)	23 (65.7%)
multi	4 (10%)	8 (20%)	10 (28.6%)
BOH	3 (7.5%)	5 (12.5%)	2 (5.7%)

p value =0.50 (comparing preeclampsia with control)

p value =0.40 (comparing Euthyroid and Hypothyroid preeclamptic women)

Table 5: Distribution according to BMI

BMI (kg/m ²)	Preeclampsia (n=40)		Control (n=35)
	Euthyroid	Hypothyroid	
< 18.5	1 (2.5%)	0 (0%)	1 (2.9%)
18.5-24.9	7 (17.5%)	6 (15%)	15 (42.9%)
25-29.9	14 (35%)	10 (25%)	16 (45.7%)
≥30	0 (0%)	2 (5%)	3 (8.5%)

p value =0.65 (comparing preeclampsia with control)

p value =0.60 (comparing Euthyroid and Hypothyroid preeclamptic women)

Table 6: Thyroid hormone and severity of preeclampsia

	Mild Preeclampsia	Severe Preeclampsia	Eclampsia
Hypothyroid	13	8	3
Euthyroid	10	4	2

p value =0.84

Table 7: Mode of delivery and severity of preeclampsia

Mode of delivery	Mild Preeclampsia	Severe Preeclampsia	Eclampsia	Control
cesarean	6	9	4	9
Vaginal delivery	17	3	1	26

p value =0.97 (comparing mild preeclampsia with control)

p value =0.0005 (comparing severe preeclampsia and eclampsia with control)

Table 8: Gestational age at birth and severity of preeclampsia

Gestational age at birth (weeks)	Mild Preeclampsia	Severe Preeclampsia	Eclampsia	control
<30	0	2	4	0
30-36	1	7	1	2
>36-40	22	3	0	33

p value =0.96 (comparing mild preeclampsia with control)

p value =0.00001 (comparing severe preeclampsia and eclampsia with control)

Table 9: Birth weight and preeclampsia

Weight of Baby	Preeclampsia (n=40)		Control (n=35)
	Euthyroid	Hypothyroid	
< 1.5 kg	1 (2.5%)	2 (5%)	0 (0%)
>1.5-2.0 kg	1 (2.5%)	3 (7.5%)	0 (0%)
>2.0-2.5 kg	6 (15%)	9 (22.5%)	3 (8.5%)
>2.5-3.0 kg	5 (12.5%)	6 (15%)	22 (62.5%)
>3.0 kg	4 (10%)	3 (7.5%)	10 (29%)

p value =0.86 (comparing Euthyroid and Hypothyroid preeclamptic women)

p value =0.00001 (comparing preeclampsia with control)

Results

Mean FT3 level was significantly lower in preeclampsia group ($p < 0.05$) and mean FT4 was comparable in both groups ($p = 0.09$). Mean TSH level was significantly more in preeclampsia women ($p < 0.05$) (Table-1). But no significant difference was observed when comparing thyroid hormonal status between the two groups ($p > 0.05$) (Table-2). Age, parity and BMI were comparable between both groups. Euthyroid and hypothyroid preeclamptic women did not have significant difference with respect to age, parity and BMI. (Tables-3, 4, 5). Thyroid hormonal levels did not correlate with severity of preeclampsia ($p > 0.05$) (Table-6). Vaginal deliveries were comparable between mild preeclampsia and control group ($p > 0.05$). Vaginal deliveries were significantly more in control group when compared to severe preeclampsia and eclampsia group ($p < 0.05$) (Table-7). Gestational age was comparable between mild preeclampsia and controls ($P > 0.05$). Gestational age was significantly lower in severe preeclampsia and eclampsia women ($p < 0.05$) (Table-8). Birth weight was not significantly different in euthyroid and hypothyroid preeclamptic women ($p > 0.05$). But birth weight was significantly lower in preeclamptic women than controls ($p < 0.05$) (Table-9).

Discussion

Prevalence of hypothyroidism in our study is 38%. Prevalence reported by Deshpande S *et al.* [8] is 17.5%. The prevalence of 2.2% is reported by others [9, 10]. Statistical difference observed in mean FT3 (low) and mean TSH (high) in this study is in agreement with others [2, 4, 8]. In preeclampsia, liver and kidney involvement may lead to decreased peripheral conversion of T4 to T3 and hence low T3 levels. This is known as low T3 syndrome [11]. Loss of proteins and protein bound hormones in urine may result in decreased low T3 levels [12]. Some studies did not find significant difference in FT3, FT4 and TSH between control and preeclampsia group [13, 14, 15]. Though mean TSH was raised in preeclampsia group, hypothyroidism was not significantly increased in preeclampsia group as compared to controls (57.5% and 42.5%) in the present study. Some overt hypothyroid women with very high TSH level in preeclampsia group have contributed to significant mean TSH levels. Our finding that hypothyroidism is not associated with increased incidence of preeclampsia is in agreement with Casey *et al.* [10]. Age, parity and BMI were comparable in both groups of women. Similar observations were reported by others [2, 8]. Casey *et al.* [10] observed hypothyroid women to be older and U Nayki *et al.* [14], found primiparity to be significant in preeclampsia women. Hypothyroidism did not correlate with severity of preeclampsia in our study. This is similar to the report of others [13, 14, 15]. Contradictory findings were reported by others [2, 3, 6]. Vaginal deliveries were significantly higher in control group in our study and it is supported by U Nayki *et al.* [14]. Birth weight and gestational age were significantly lower in preeclampsia group but no difference was observed between euthyroid and hypothyroid preeclamptic women. Same findings were noted in other study [12]. So LBW observed in preeclampsia may be due to placental dysfunction and severity of preeclampsia necessitating termination and not due to hypothyroidism. No correlation with birth weight and hypothyroidism was reported by others [4, 14]. On the contrary others reported negative correlation between birth weight and TSH levels [3, 6].

Conclusion

According to this study hypothyroidism is not significantly associated with preeclampsia. The role of hypothyroidism in preeclampsia is controversial in the published reports. Limitation of our study is the small sample size and as it was done at term gestation, we were unable to find the association of hypothyroidism as a predictor of preeclampsia. Further large randomized double blind studies in all ethnic, geographic groups are needed to prove that hypothyroidism may be a predictor of preeclampsia. But hypothyroidism in pregnancy is associated with some adverse effects in the published reports. So screening for hypothyroidism in pregnancy and replacement of thyroid hormones in indicated women will improve the obstetric outcome in future.

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethical committee

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