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To Study The Association of Thyroid Hypofunction With Increasing Age in Pregnant Women With Hypertension

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Abstract

Objectives: To study the association of thyroid hypofunction with increasing age in pregnant women with hypertension

Design: Prospective, observational, cohort study.

Setting: Study was carried out in Department of Obstetrics and Gynaecology, S.S.M.C and associated G.M. Hospital Rewa, Madhya Pradesh during the period of 1st August 2015 to 31st July 2016.

Study Population: In the study 200 women were recruited in which 100 women were taken as cases and 100 were taken as control. Study population was selected randomly from women visiting to the outdoor and those admitted in antenatal ward.

Participants: Cases: Women visiting the outdoor or those admitted in antenatal ward with diagnosis of gestational hypertension or preeclampsia where the case was defined on the basis of inclusion and exclusion criteria

Controls: Women visiting the outdoor or those admitted in antenatal ward without gestational hypertension or preeclampsia.

Main Outcome Measure(s): Results: Incidence of hypothyroidism increased with age from 12.5%(1 out of 18), to 12.8%(6 out of 47), then to 41.9%(13 out of 31) and then further to 50%(7 out of 14) in age group <20 years, 20-24 years, 25-29 years and ≥ 30 years respectively.

Conclusions: A positive association is present between increasing age and incidence of hypothyroidism (clinical and subclinical) in antenatal patients having hypertension. This shows that the incidence of hypothyroidism increases with age in women with hypertension in pregnancy and age is significantly

associated with hypothyroidism in the study group. Keywords: Hypertension, Thyroid Hypofunction, Gestational Hypertension, Preeclampsia

Introduction

Thyroid dysfunction constitutes one of the commonest endocrine disorders during pregnancy after diabetes mellitus [1]

Preeclampsia (PE) and gestational hypertension (GHTN) are new onset hypertensive disorders in pregnancy, occurring after mid-gestation after 20 weeks of gestation up to 6 weeks postpartum in previously normotensive non-proteinuric pregnant women with proteinuria (more than 300 mg/l in 24 hours specimen) and without proteinuria respectively[2]. They affect up to 5–15% of pregnancies and are important risk factors for maternal and fetal morbidity and mortality [3] Pregnancy is associated with profound modifications in the regulation of thyroid function. These changes are the result of the various factors like an increase of thyroid-binding globulin (TBG) due to elevated estrogens and human chorionic gonadotropin (HCG), increased renal losses of iodine due to increased glomerular filtration rate, modifications in the peripheral metabolism of maternal thyroid hormones and modifications in iodine transfer of placenta. Hypothyroidism is also a well-known side-effect of anti-VEGF treatment due to capillary regression in the thyroid tissue. Although, pregnancy is usually associated with very mild hyperthyroxinemia which is the presence of free thyroxine (FT4) value above the 2.5th percentile with a thyrotropin (TSH) level within the reference range [4], but women complicated with preeclampsia have high incidence of hypothyroidism that might correlate with the severity of preeclampsia. Long term thyroid dysfunction may result from the effects of exposure to anti-angiogenic factors during pregnancy complicated by preeclampsia or gestational hypertension. Thyroid dysfunction in early pregnancy has also been associated with the development of preeclampsia and gestational hypertension in some studies, but not in all.

Women with subclinical hypothyroidism identified during pregnancy have an increased risk for severe preeclampsia when compared with euthyroid women. Hence, thyroid function tests should be performed in all pregnant women with hypertension during pregnancy.

Objective

To study the association of Thyroid Hypofunction with increasing age in pregnant women with hypertension.

Methodology

Study Design: Prospective observational Cohort study.

Study Centre: Shyam Shah Medical College & Gandhi Memorial Hospital, Rewa.

Study Population: In the study 200 women were recruited in which 100 women were taken as cases and 100 were taken as control. Study population was selected randomly from women visiting to the outdoor and those admitted in antenatal ward.

Inclusion & Exclusion Criteria

Inclusion Criteria:

1. Pregnant women with age 17-35 years.
2. Pregnant women with gestational age above 20 weeks.
3. Women with pregnancy induced hypertension.
4. Women with no other systemic illness.
5. Women with single intrauterine gestation

Exclusion Criteria:

1. All pregnant women with history of thyroid disease (hypo or hyperthyroidism, goitre, grave's disease, autoimmune and toxic nodular thyroiditis etc.)
2. Systemic disorders (diabetes, renal disease, epilepsy or other convulsive disorders, chronic hypertension, autoimmune and collagen vascular diseases)

3. Multiple pregnancy.
4. H/o intake of any medication that might affect thyroid function, drugs like glucocorticoids, phenobarbitone, levothyroxine, methimazole, propylthiouracil and other anti-thyroid medications.
5. Pregnant women with gestational age <20 weeks.
6. Cases and controls lost on follow-up

Study Period: From 1st August 2015 to 31st July 2016.

Case: Women visiting the outdoor or those admitted in antenatal ward with the diagnosis of gestational hypertension or preeclampsia, where the case was defined on the basis of inclusion and exclusion criteria. Preeclampsia is a pregnancy specific syndrome characterized by elevation of blood pressure of more than 140mm of Hg systolic or more than 90mm of Hg diastolic with proteinuria (more than 300 mg/l in 24 hours specimen) after 20 weeks of gestation in previously normotensive non-proteinuric pregnant women. Gestational hypertension is characterized by new onset elevation of blood pressure of more than or equal to 140mm of Hg systolic or more than or equal to 90 mm of Hg diastolic after 20 weeks of gestation in absence of proteinuria.

Control: The control constituted of equal number of matched age, parity, socio-demographic status, gestational age; healthy normotensive pregnant women visiting the outdoor or those admitted in antenatal ward.

Method of Study

Written informed consent from all participants recruited in study was taken after they had been made aware of purpose of study. Particulars of the women were noted such as name, age, symptoms, menstrual history for menarche, last menstrual period and past menstrual cycles, history of present pregnancy. Both cases and controls were classified into upper, middle, and lower socio economic status. Past obstetric history was asked

for duration of marriage, infertility, gravidity and parity status, recurrent abortions, preeclampsia, growth restriction, low birth weight, preterm delivery, prematurity, late pregnancy losses, neonatal deaths, and mental retardation in previous pregnancy. Past medical history was asked for any associated medical disorders like diabetes, thyroid disorders, exposure to radiation or autoimmune disorders. Significant surgical history and family history was also asked. A thorough clinical examination including height, weight, pulse, blood pressure, pedal edema, thyroid enlargement etc. was done followed by systemic examination. In obstetric examination fundal height, presentation and amount of liquor was noted and fetal heart sound was auscultated with stethoscope.

Investigations

All preliminary and baseline investigations like complete blood count, blood grouping and typing, urine routine and microscopy, HBsAg, HIV and blood sugar were done along with USG. Ultrasonography was done for fetal growth, liquor and placenta. All investigations pertaining to the complications of preeclampsia were also done like liver and kidney function tests, serum uric acid, platelet count and after that thyroid function test was performed.

Procedure

Assessment of thyroid status of cases and control was done with serum Free T3, T4 and TSH, for which 10ml venous blood sample was taken from the cubital vein irrespective of status of last meal, test was done before the initiation of any treatment and before the delivery. All samples were sent to the laboratory where sera was separated and stored at -200C until assayed. Free T3 (tri-iodothyronine), free T4 (thyroxine) and TSH (thyroid-stimulating hormone) were measured using fully automated chemiluminescence system (CLIA kits). Further, depending upon the FT4 and FT3 values all women were classified as follows.

Classification according FT3, FT4 and TSH levels:

Functions	TSH	Free T3	Free T4
Clinical hypothyroidism	Elevated	Low	Low
Subclinical hypothyroidism	Elevated	Normal	Normal
Euthyroid	Normal	Normal	Normal
Subclinical hyperthyroidism	Low	Normal	Normal
Clinical hyperthyroidism	Low	Elevated	Elevated

Guidelines for trimester specific serum TSH levels

(Recommended by American Thyroid Association Taskforce on Thyroid Disease during Pregnancy and Postpartum)[5]

Recommended Trimester Specific TSH levels:

Trimester	FT3	FT4	TSH
First Trimester	1.91-3.5 pg/ml	0.86-1.77 pg/ml	0.1 to 2.5 pg/ml
Second Trimester	2.8-4.2 pg/ml	0.63-1.29 pg/ml	0.2 to 3.0 pg/ml
Third Trimester	2.4-4.1 pg/ml	0.66-1.12 pg/ml	0.3 to 3.0 pg/ml

Statistical analysis: The data of the study were entered and analysed using the software Microsoft Excel 2013 for windows. Appropriate univariate and bivariate analysis were carried out using the Student t test for the continuous variable / proportion test (z test / t test) and two-tailed Fisher exact test or chi-square (χ^2) test for categorical variables. The critical levels of significance of the results were considered at 5% i.e. $P < 0.05$ was considered significant.

Results

Majority of women with pregnancy induced hypertension were having mild preeclampsia (63%) followed by severe preeclampsia (23%) and gestational HTN (14%)(Table No.1) Majority of women in study group (73%) as well as in control group (89%) were Euthyroid (EU). In the

study group, cases of sub clinical Hypothyroidism (SCH) as well as clinical Hypothyroidism (CH) were more in comparison to control group. No cases were hyperthyroid (HYPER) in study as well as in control group. (Table No. 2) In the study group and control group maximum number of women were between 20-29 years of age as this is the predominant age of reproduction.

Incidence of thyroid hypofunction increases with increasing age in both groups. In the study group incidence of hypothyroidism increased with age from 12.5%(1 out of 18) ,to 12.8%(6 out of 47), then to 41.9%(13 out of 31) and then further to 50%(7 out of 14) in age group <20 years, 20-24 years, 25-29 years and ≥ 30 years respectively i.e. a positive association is present between increasing age and incidence of hypothyroidism.

Table 1: Distribution of cases according to severity of hypertension

PIH	Study group n=100 (%)
Gestational hypertension (GHTN)	14
Mild preeclampsia	63
Severe preeclampsia	23
Total	100

Table 2: Distribution of cases according to thyroid status

Thyroid Status	Study Group (N=100)	Control Group (N=100)
EU	73	89
SCH	23	10
CH	4	1
HYPER	0	0
TOTAL	100	100

Table 3: Distribution of cases with thyroid disorders according to age (in year)

Age Group	Study Group (n=100)				Control Group (n=100)			
	EU	SCH	CH	TOTAL	EU	SCH	CH	TOTAL
<20	7	1	0	8	5	0	0	5
20-24	41	6	0	47	67	3	0	70
25-29	18	11	2	31	16	7	1	24
≥30	7	5	2	14	1	0	0	1
TOTAL	73	23	4	100	89	10	1	100

($\chi^2=17.192, P=0.0086$) ($\chi^2=16.650$ $P=0.0107$)

Discussion

In our study, maximum number of women were between 20-29 years of age in study group (80%) and control group (94%) as this is the predominant age of reproduction.

Incidence of thyroid hypofunction increases with increasing age in both groups. Among the cases in the present study, incidence of hypothyroidism increased with age from 12.5% (1 out of 18) to 12.8% (6 out of 47), then to 41.9% (13 out of 31) and then further to 50% (7 out of 14) in age group <20 years, 20-24 years, 25-29 years and ≥ 30 years respectively.

Comparable to our study, G. Shobha et al (2005) [6], showed that incidence of thyroid hypofunction increases with increasing maternal age.

Allan et al (2000) [7] and Vaidya et al (2007) [8] also found that increasing maternal age is a risk factor for hypothyroidism.

Conclusions

A positive association is present between increasing age and incidence of hypothyroidism (clinical and subclinical) in antenatal patients having hypertension. This shows that the incidence of hypothyroidism increases with age in women with hypertension in pregnancy and age is significantly associated with hypothyroidism in the study group.

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