Original Article

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A Prospective Study of Routine Screening of Hypothyroidism in Antenatal Patients and their Outcome with Levothyroxine Treatment

Obstetrics and Gynaecology Section

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ABSTRACT

Introduction: Pregnancy with hypothyroidism is associated with significant maternal, fetal and neonatal complications. Early diagnosis and treatment can effectively reduce such complications.

Aim: To find out the complications that can be prevented or reduced in severity in adequately treated hypothyroid pregnant women.

Materials and Methods: Pregnant women attending obstetrics' OPD upto 20 weeks were screened with serum Thyroid Stimulating Hormone (TSH) and free Thyroxine FT4 .Those having Subclinical Hypothyroidism (SCH), Overt Hypothyroidism (OH) and pre pregnant women with hypothyroid were treated with levothyroxine as per consulting with endocrine unit. They were followed up till delivery and any adverse outcomes were documented such as Pregnancy Induced Hypertension (PIH), Pre Eclamptic Toxemia (PET), Abruption, Preterm Premature Rupture Of Membranes (PPROM), Low Birth Weight (LBW), oligohydramnios, Gestational Diabetes Mellitus (GDM), abortion, Intra Uterine Death (IUD), mode of delivery and Neonatal Intensive Care Unit (NICU) admission were compared with similar complications documented among normal pregnant women excluding the treated hypothyroid during a period of one year study. Untreated or late trimester diagnosed hypothyroidism were excluded from study group.

Results: Incidence of PIH, GDM, Oligohydramnios, PPROM, NICU admissions and caesarean section were higher among hypothyroid pregnant women though adequately treated than the control pregnant women. But incidence of LBW baby is less and no one had developed PET, Eclampsia or abruption among treated group. Comparing between SCH and OH incidence of PIH is almost equal in both while association of GDM is more in OH. A p-value for PIH, GDM, Oligohydramnios, PPROM developed in hypothyroid pregnant ladies which were calculated by Yates corrected Chi-Square and Fisher's-exact test from open epic version 3.03a. A p-value is significant (<0.001) for PIH, GDM, PPROM and oligohydramnios but insignificant for LBW.

Conclusion: Severe form of PIH (PET and Eclampsia), IUD and Abruptio placentae can be prevented in adequately treated pregnant hypothyroid women and all pregnant women with SCH and OH must screen for GDM even if there is no other risk factors for GDM.

Keywords: Abruptio placentae, Overt, Pregnancy induced hypertension, Preterm premature rupture of membranes, Subclinical

INTRODUCTION

The health of both mother and children pre and post delivery is being affected by thyroid disease during pregnancy. Thyroid dysfunction in pregnancy both in subclinical and overt hypothyroidism has adverse effects on maternal and perinatal outcome. The deleterious effect of uncorrected thyroid dysfunction can adversely affect neuropsychological development of child [1].

Pregnancy has a profound impact on the thyroid gland and thyroid function. The gland increases 10% in size during pregnancy in iodine replete countries and 20 to 40% in iodine deficiency countries. Simultaneously there is an increase in synthesis of Thyroxin and Tri-idothyronine by 50% and 50% increase in iodine requirement. Pregnancy in fact act as a stress test for thyroid, resulting in hypothyroidism in women having limited thyroid reserve or iodine deficiencies and postpartum thyroiditis develops in women with underlying Hashimoto's disease who were euthyroid prior to conception [2].

Increase number of women found to have thyroid dysfunction on universal screening rather than screening selectively those is at high risk of thyroid problems [3]. A study by Vaidya et al., revealed screening only high risk pregnant women miss 30% of hypothyroid women [4]. Yet the most effective method of screening for thyroid dysfunction is not known [3]. Assessment of serum TSH is found to be most used thyroid screening during pregnancy.

Several trials mostly retrospective have proved that both overt and subclinical hypothyroidism during pregnancy affect both maternal and fetal complications like anaemia [3], miscarriage, fetal death [5,6], abruption [7], GDM [8,9] low birth weight, preterm birth [7,10], pre eclampsia [11,12], still birth, preterm birth [13], hypertension in pregnancy [14] and increase neonatal respiratory distress [3,15]. But few research materials have indicated the adverse pregnancy outcomes can be prevented in women with adequately treated thyroid diseases or these are due to disease process itself. Therefore the study was carried out to find out incidence of SCH and OH in pregnant women in our locality and adequately treating them so that we can prevent or reduce the severity of obstetric complications that develops due to them.

MATERIALS AND METHODS

This is a prospective study conducted in Obstetrics and Gynaecology department of IMS and SUM Hospital Bhubaneswar, Odisha, India, during a period from August 2015 till July 2016. Institutional Ethical clearance was taken for this study. Total number of 4031 pregnant females attending OPD for the first time upto 20 weeks during this period was included in this study group after undertaking written consent from them irrespective of their age, parities, BMI, history of infertility or diabetes mellitus or any other risk factors for development of hypothyroidism. Those who were diagnosed to have hypothyroid before pregnancy were also included in this study group. Patients who were diagnosed to have raised TSH in late trimester or untreated were excluded from study. Routine screening

of serum TSH and FT4 were performed in all patients of the study group. Previous TSH and FT4 values were collected from those who were pre pregnancy diagnosed cases of hypothyroidism. According to The American Thyroid Association (ATA) guide line those who are diagnosed to have SCH and OH during pregnancy and already pre pregnany diagnosed case of hypothyroid were treated with levothyroxine 1.6 mcg per kg per day and dose was adjusted by 12.5 to 25 mcg increase every 4 to 6 weeks until the patient was euthyroid and serum TSH returned normal as per consultation with Endocrinology unit. These patients were followed up till deliveries and their adverse obstetrical outcomes were recorded as development of PIH, LBW, Oligohydramnios, association with GDM, PPROM and NICU admission. These adverse outcomes were compared with similar types of complications developed in 3213 number of pregnant ladies delivered in our hospital from August 2015 till July 2016 excluding those treated hypothyroid patients taken as control group.

Subclinical hypothyroidism is defined as raised thyrotropin combined with a normal serum free thyroxine level. The ATA 2011 and Endocrine Society (ES) 2012 guidelines recommended that the normal thyrotropin reference range should be 0.1-2.5miu/ml in first trimester, 0.2-3miu/ml, .3-3.5miu/ml in second and third trimester respectively [2,16]. The ATA, ES, AACE (American Association of Clinical Endocrinologist) have recommended and generally accepted that any pregnant women having thyrotropin above 10miu/ml and normal thyroxin level should be diagnosed as overt Hypothyroidism [2,16,17]. Subclinical hypothyroidism is a biochemical diagnosis and cannot be based upon patient's symptoms, hence routine TSH screening is best method for diagnosis of hypothyroidism. Worldwide endemic iodine deficiency accounts for most cases of hypothyroidism in pregnant women while chronic autoimmune thyroiditis is the most common cause of hypothyroidism in iodine sufficient parts of the world [18].

In this one year study 256 pregnant ladies were diagnosed to have hypothyroid by routine screening of TSH and FT4 by chemi illumisence method (CLA) by Roch Cobas 411e in our Hospital's central laboratory up to 20 weeks of gestation irrespective of their gravida. CLA is more sensitive as well as more specific for monitoring thyrotropin [19,20]. All diagnosed cases of hypothyroid pregnant ladies were treated with levothyroxine dosage adjusted by Endocrinologist and were followed up with serum TSH and FT4, in 4 to 8 week intervals. Out of 256 patients 38 were lost follow up and ultimately 218 hypothyroid pregnant females were followed up till deliveries and their outcomes were recorded. Total number of deliveries in our hospital in one year was 3431 and the incidence of hypothyroidism in pregnancy was calculated to be 6.35%.

STATISTICAL ANALYSIS

Statistical significance was taken at the 0.05 value. Categorical variables were compared using the χ^2 test and Fisher's-exact test was used when there were few observations. A p-value for PIH, GDM, Oligohydramnios, PPROM developed in hypothyroid pregnant ladies which were calculated by Yates corrected Chi-square and Fisher's-exact test from open epic version 3.03a.

RESULTS

In our study [Table/Fig-1], indicates the incidence of adverse obstetrical outcomes in the treated hypothyroid pregnant ladies as well as incidence of similar adverse outcome among all delivered patients. Out of these 184 was Sub Clinical Hypothyroid and 34 were Overt Hypothyroid. Incidence of PIH, GDM, Oligohydramnios,

Complication	No. of Patients	Percentage %	No. of Patients	Percentage %
	Treated Patients		Control Patients	
PIH	35	16.05	171	5.3
GDM	22	10	41	1.27
Oligohydraminous	24	11	185	5.8
PPROM	13	5.9	62	1.9
Low birth weight	13	5.9	481	14.9
NICU Admission	12	5.5	219	6.8
Pre-eclampsia	0	-	75	2.3
Abortion	2	0.91	-	-
Abruptio	0	-	-	-
IUD	0	-	-	-

[Table/Fig-1]: Percentage of complications developed in treated (218) and control (3213) hypothyroid pregnant ladies.

Mode of Delivery	Treated Hypothyroid Patients (218)		Control Patients (3213)	
NVD	80	36.26%	1869	58.1%
LSCS	136	62.3 %	1344	41.8%
ABORTION	2	0.9 %	-	-

[Table/Fig-2]: Results of caesarean section among treated hypohyroid patients and control patients.
NVD- Normal Vaginal delivery, LSCS= Lower segment Cesarian section

Complications	Subclinical Hypothyroidism (184)		Overt Hypothyroidism (34)	
PIH	27	14.6%	8	23.5%
LBW	22	11.9 %	4	11.7%
GDM	16	8.6 %	6	17.6%
Oligohydraminous	23	12.5 %	1	2.9%
PPROM	11	5.9 %	2	5.8%
Abortion	2	1.08 %	0	-
Abruptio	-	-	-	-

[Table/Fig-3]: Incidence of adverse outcomes between SCH and OH.

Treated Hypothyroid Patients	Normal	TP	Marginal Row Tools	Yates corrected Chi square value	p-value
PIH +ve	171 (192.91) {2.49}	35 (13.09) {36.68}	206	39.79	<0.001
PIH –ve	3042 (3020.09) {0.16}	183 (204.91) {2.34}	3225		
LBW +ve	481 (474.79) {0.08}	26 (32.21) {1.2}	507	1.27	0.130
LBW –ve	2732 (2738.21) {0.01}	192 (185.79) {0.21}	2924		
Oligohydramnios +ve	185 (195.72) {0.59}	24 (13.28) {8.65}	209	8.945	0.0013
Oligohydramnios –ve	3028 (3017.28) {0.04}	194 (204.72) {0.56}	3222		
GDM +ve	41 (59) {5.49}	22 (4) {80.91}	63	83.2	<0.001
GDM –ve	3172 (3154) {0.1}	196 (214) {1.51}	3368		
PPROM +ve	62	13	75	Fisher-exact test 13.71	<0.001
PPROM –ve	3151	205	3356		

[Table/Fig-4]: A p-value of treated hypothyroid patients.
Yates corrected chi-square and Fisher's-exact test were applied
Values within bracket ( )-expected cell totals
Values within bracket { }- Chi-square statistic for each cell

PPROM, NICU admissions were higher among hypothyroid pregnant women though adequately treated with levothyroxine than the total delivered pregnant women (3213). But incidence of LBW babies were less and no one had developed PET or Eclampsia, abruption and IUD among the treated group while incidence of PET and Eclampsia was 2.3% in control group. Incidence of PIH and GDM were very high (16% and10% respectively) in treated thyroid group than the control (5.3% and1.27% respectively).Two cases of abortion were documented while not a single case of IUD was documented among treated women.

In our study rate of cesarean section was more in treated thyroid group [Table/Fig-2].

[Table/Fig-3] indicates that among the hypothyroid patients 184 were SHC and 34 were OH whose TSH were >10miu/ml or above the trimester specific reference with decrease FT4 level. Comparing the adverse obstetric outcomes between SCH and OH, the incidence of LBW is almost equal in both the groups while associations of GDM and PIH incidence are more among OH. Considering the age group for hypothyroidism among pregnant women is higher between 26-30 years because maximum pregnant ladies were in this age group according to hospital records.

Our study shows the p-value for PIH, GDM, Oligohydraminos, PPROM developed in hypothyroid pregnant ladies which were calculated by Yates corrected chi-square and Fisher's-exact test from open epic version 3.03a. A p-value was significant (<0.001) for PIH, GDM, PPROM and oligohydramnios but insignificant for low birth weight [Table/Fig-4].

DISCUSSION

Pregnancy has a profound impact on thyroid gland and its functions which warrants universal screening for hypothyroidism in all pregnant women. Hypothyroidism poses special risk for both pregnant women and her developing foetus. Early detection by screening all pregnant ladies with TSH and treating them with levothyroxine can be able to prevent complications to some extent. It is better to screen for hypothyroid both pregnant women and those who wants to be pregnant as thyroid hormone status is directly related to foetal brain development.

In different prospective studies the prevalence of undiagnosed subclinical hypothyroidism ranges from 3 to 15 % [21]. In International evidences, the estimated prevalence of hypothyroidism in pregnancy was 2-3% [22,23]. Of these, 0.3-0.5% is OH and 2-2.5% is SCH [24]. Prevalence of hypothyroidism in pregnancy in Indian population is 4.8-12% [24]. Reported prevalence by Sahu et al., in 2010 was 6.47% with 4.58% as OH [25]. Another Indian study has reported the prevalence of hypothyroidism to be 12%, of which 3% was OH and 9% was SCH [26]. In our study the incidence of hypothyroidism was 6.35% of which 5.35% was SCH and1.01% was OH which indicates higher prevalence of SCH and OH like other Indian studies.

Though the previous data suggests hypothyroid mothers have increased incidence of pregnancy related complications if it is not corrected or inadequately treated [11,12,27], but no data suggests reduced or increased risk of complications in adequately treated SCH/OH mothers. However, one study Matalon S et al., had shown increase risk of caesarean section in cases with adequately treated hypothyroidism [28]. A register based study without estimate of treatment adequacy found increase risk for preeclampsia, diabetes, preterm births, caesarean section, and labour inductions among those on levothyroxine use [29]. Study done by Avalovich et al., in inadequately treated hypothyroid pregnant mother the incidence of preterm deliveries was 20% among OH and 7.2% among SCH [5]. But in our study with adequately treated mother incidence of PPROM leading to preterm deliveries are almost equal in both OH and SCH (5.9 in SCH and 5.8 in OH). This implies the incidence of preterm is reduced in controlled patient. Similarly study done by Leung et al., incidence of PIH was 36% in OH and 25% in SCH among untreated hypothyroid mother while in our study in controlled patient incidence of PIH was 23.5% and 14.6% in OH and SCH respectively which is reduced incidence among treated patients [12].

The most common endocrinology problems during pregnancy are GDM and hypothyroidism. Approximately 1.1 to 14.3% of pregnant ladies suffer from GDM and hypothyroidism affects 2.6 to 6.4% of them [30]. In our study there was clear-cut association of increased incidence of GDM among hypothyroid and that to higher among OH (17.6%).

LIMITATION

Sample size was small and it could have been better to compare the obstetric complications between treated and untreated pregnant women.

CONCLUSION

It has already been proved that thyroid diseases are associated with various obstetrical, labor and delivery complications. ATA and ES have already recommended routine TSH screening in all pregnant women but we lack the information whether all these adverse pregnancy outcomes can be avoided by adequately treating hypothyroid pregnant women with levothyroxine or not. We concluded from our study that even if pregnancy with hypothyroidism adequately treated with levothyroxine, development of adverse outcomes cannot be totally prevented. However incidence of PIH, Preterm delivery can be reduced as well as severe form of PIH (PET and Eclampsia), IUD and Abruptio placentae can be prevented among controlled hypothyroid pregnant women. All hypothyroid pregnant women must be screened for GDM as incidence of GDM is higher among them. However, further researches are needed to prove the fact.

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