International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Radha KR et al. Int J Reprod Contracept Obstet Gynecol. 2017 Mar;6(3):781-786
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20170470

Original Research Article

Do we need to screen and treat pregnant women for subclinical hypothyroidism? A cross sectional study in a rural tertiary centre in Kerala, India

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Received: 04 January 2017
Revised: 06 January 2017
Accepted: 27 January 2017

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ABSTRACT

Background: Hypothyroidism (HT) is associated with maternal and perinatal morbidity. Subclinical HT rather than overt occur in pregnancy, because overt HT causes infertility. Treatment of overt HT was beneficial in reducing the fetal and maternal complications, Usefulness of correcting subclinical hypothyroidism was doubtful, hence Universal screening of pregnant women was not recommended.
Methods: Cross sectional study, conducted in the department of obstetrics and gynecology, Government Medical College, Thrissur, Kerala, India. 50 consecutive cases of subclinical hypothyroidism in pregnancy were analyzed for Thyroid function, antenatal, natal, postnatal complications. Perinatal complications, including neonatal hypothyroidism also noted. Statistical analysis done using computer software Epi info3.4. Data expressed in its frequency and percentage, continuous data in mean.
Results: All women in the study group received levothyroxine during pregnancy from time of diagnosis. At the time of delivery 84% women were euthyroid and 16% hypothyroid. Complications like anemia 36%, abruption 4%, and postpartum hemorrhage 6% showed a statistically significant association, while pre-eclampsia 20%, preterm labor 22% had no statistically significant association. Comparing the women who are euthyroid as a result of levothyroxine supplementation to women inadequately treated, complications like anemia (33% versus 50%, p value 0.042), abruption (0% versus 4%, p value0.023), PPH (2% versus 6%, p value 0.014) were significantly less in well controlled.
Conclusions: Significant association was noted between inadequately treated hypothyroidism and maternal complications like anaemia, placental abruption, placenta previa, PPH, preterm delivery, and caesarean section rate for foetal distress. Universal screening of pregnant women for thyroid status is recommended.

Keywords: Maternal morbidity, Perinatal outcome, Subclinical hypothyroidism

INTRODUCTION

Thyroid disease is the second commonest endocrine disorder next to diabetes mellitus affecting women of child bearing age.[1] About 2-5% of all pregnant women are reported to have some degree of hypothyroidism.[2] Overt hypothyroidism complicates 2-3 per 1000 pregnancies.[3] Subclinical hypothyroidism is a prevalent condition which may go unrecognised and has the potential to develop adverse maternal and fetal outcome.[4]

Thyroid hormone plays a vital role in development of placenta and fetus.[5] In early pregnancy the embryo depends on maternal thyroid supply via placenta. Foetal

thyroid functions start at 10 -12 weeks of gestational age.[6] Maternal thyroxin accounts for 30% of thyroxin in foetal serum at term.

Overt hypothyroidism is diagnosed when an abnormally high thyrotropin level was accompanied by low thyroxin level.[7] Sub clinical hypothyroidism defined as elevated serum thyrotropin level accompanied by normal serum thyroxin concentration. TSH plays a central role in screening and diagnosis of hypothyroidism. The thyroid adapts through changes in thyroid hormone economy and in the regulation of the hypothalamic-pituitary-thyroid axis.[8] Both the lower normal limit and the upper normal limit of serum TSH are decreased by about 0.1 - 0.2 mIU/L and 1.0 mIU/L, respectively, compared with the customary TSH reference interval of 0.4-4.0 mIU/L of nonpregnant women. Serum TSH and its reference range gradually rise in the second and third trimesters, but it is noteworthy that the TSH reference interval remains lower than in nonpregnant women.[9] Hypothyroidism in pregnancy is diagnosed where TSH value is in the following range in each of the trimesters : first trimester, 0.1-2.5 mIU/L; second trimester, 0.2 - 3.0 mIU/L; third trimester, 0.3-3.0 mIU/L.[9,10]

Pregnancy complications with hypothyroidism include increased incidence of preeclampsia, abruptio placentae, anemia, and preterm labour.[2,3] Unexplained still birth, fetal distress, low birth weight, neonatal hypothyroidism are perinatal complications.[2,3] Women with previously diagnosed hypothyroidism already on thyroxin replacement therapy, when pregnant need dose increment.[11] Treatment of overt hypothyroidism is proven to be beneficial in eliminating maternal and fetal complications.[11] Most thyroid dysfunction that occurs in pregnancy is subclinical. But the lack of clear data for efficacy of treatment of sub clinical hypothyroidism, controversy exists regarding the need for universal screening for thyroid dysfunction during pregnancy verses testing only symptomatic or high risk women.[11,12]

Various guidelines like American Association of Clinical Endocrinologist and the American thyroid Association 2012, Endocrine society 2012, The Cochrane Collaboration 2010, ACOG does not recommend universal screening for thyroid disease.[9,10,12,13] Targeted thyroid function testing of pregnant women at high risk for thyroid disease only would miss about one third of women with overt and sub clinical thyroid disease.[14,15]

METHODS

This was a cross sectional study conducted in the Department of Obstetrics and Gynecology, Government Medical College, Thrissur, Kerala, India over a period of one year. Objective of the study was to analyze maternal complications and perinatal outcome of women diagnosed to have subclinical hypothyroidism and also to determine the occurrence of neonatal hypothyroidism among the neonates of these women.

All pregnant women detected to be hypothyroid prior to or during pregnancy and were biochemically euthyroid or hypothyroid were included in the study. Women with multiple pregnancy, IUGR, and overt diabetes, history of thyroid surgery were excluded from study. Assuming the prevalence rate of hypothyroidism between 3-5% in pregnant women a sample size of 50 was taken. Diagnostic criteria was decided according to the endocrine society (USA) guidelines. According to these criteria, women with increased TSH (upper limit 10mIU/l) and normal T3, T4 Value is classified as having sub clinical hypothyroidism and those with increased TSH and low T3, T4 is termed as overt hypothyroidism. TSH value of 10 mIU/L or greater with normal T3, T4 was included in overt hypothyroidism. In neonate TSH value of >20 is considered abnormal who is tested after 72 hours of birth.[16] All details of women were collected on a structured questionnaire after getting their consent. Age, parity, socioeconomic status, BMI, were noted. Details age of present pregnancy like duration of pregnancy, occurrence of gestational hypertension, preeclampsia, PPROM, abruption, placenta previa. Apart from routine investigations all are tested for thyroid function. Initial dose of thyroxin, need for increasing dose, discontinuation of drug during pregnancy, thyroid status at time of delivery were also noted. Women are followed up till delivery. Gestational age at delivery, mode of delivery, indication for caesarean section, maternal and fetal outcome were noted. After delivery neonatal examination was done to determine the APGAR score, gestational age, birth weight, fetal growth restriction, congenital anomalies. Neonatal thyroid status was checked after 72 hours of delivery.

Statistical analysis was done using Epi info 3.4. Data are expressed in its frequency and percentage. Continuous data are expressed as mean (standard deviation). To elucidate the associations and comparisons between different parameters chi square test, and Fishers test were used as non-parametric test wherever possible. Data was compared with our hospital statistics for the general obstetric population.

RESULTS

The total no of obstetric admission in the study period of one year in the hospital was 2794 out of which 71 had thyroid function abnormality (which include both overt and sub clinical hypothyroidism) making a prevalence of hypothyroidism in pregnancy as 2.54%. Out of these 71 women 50 were having subclinical hypothyroidism and data of these women were analysed. The distribution of socio demographic variables like age, parity, BMI of the study group shown in Table 1.

90% of women were within 20 to 34 years, of them 46% of the subjects were primigravida and 54% were multigravidae. Among the 50 patients, 32% of the women are overweight and 10% obese. 26 women (52%) were found to be hypothyroid during pregnancy while 24

(48%) were hypothyroid on treatment before pregnancy (confirmed with their initial investigation records). Fifteen women (62.5%) who were already on replacement therapy needed dose increment. The mean thyroxin dose increment required was 65.5 mg to103 mg. In 42 women (84%) hypothyroidism was well controlled with treatment and were euthyroid at the time of delivery (Figure 1). Among the 8 women (16%) who were hypothyroid at time of delivery, three of them had discontinued treatment and in the remaining five women, hypothyroidism was detected recently and the women delivered within one month of treatment. The obstetric outcomes of euthyroid and hypothyroid women at the time of delivery were compared. On analysing the past obstetric events in the 27 multigravidae, 13 women (48.1%) had experienced adverse pregnancy outcome in the previous pregnancies namely miscarriage 44.4% and still birth 3.7%. Among these 50 patients, 12% had taken treatment for infertility. The maternal complication in the present pregnancy of these 50 women encountered were analysed. Anemia (36%), preeclampsia (20%), preterm delivery (22%) were the commonest maternal complication noted (Table 2). The association between anaemia in relation to the thyroid status at delivery showed that 36% of hypothyroid women were anaemic out of which 16% had mild anaemia and 20% moderate anaemia. 3 had resistant anaemia not responding to parenteral iron therapy.

Table 1: Age, parity and body mass index of women with hypothyroidism.

Variables		Frequency n=50	Percentage
Age of the women (years)	<20	2	4%
	20-24	11	22%
	25-29	22	44%
	30-34	12	24%
	>35	3	6%
Parity	Primi	23	46%
	Para 1	21	42%
	Para 2	4	8%
	Para 3	2	4%
BMI	Normal	29	58%
	Over weight	16	32%
	Obese	5	10%

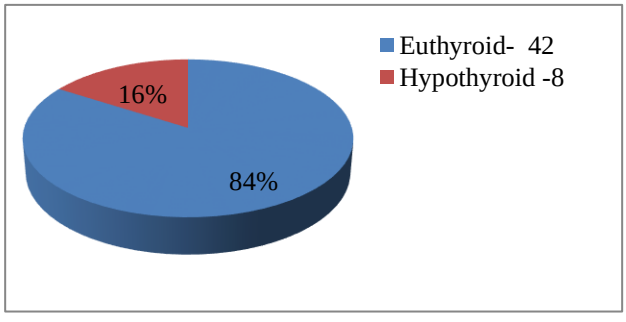

Figure 1: Thyroid control at delivery.

The occurrence of anaemia among euthyroid and hypothyroid women in the group were compared and it was found that 50% of hypothyroid women and 33% of Euthyroid women had anaemia, which was found to be statistically significant with a p value 0.042 (Table 3).

Table 2: Maternal complications in pregnant hypothyroid women.

Complications	Number of women n = 50	Percentage
Anaemia	18	36%
Gestational hypertension	3	6%
Preeclampsia	10	20%
Placental abruption	2	4%
Placenta previa	2	4%
Preterm delivery	11	22%
Postpartum hemorrhage	3	6%

Table 3: Thyroid status and anaemia.

Thyroid status	Anaemia status		Total
	Not anaemic	Anaemic	
Euthyroid (42)	28 (66.7%)	14 (33.3%)	42 (100%)
Hypothyroid (8)	4 (50%)	4 (50%)	8 (100%)
Total	32 (64%)	18 (36%)	50 (100%)

P value 0.042

The occurrence of preeclampsia in the euthyroid and hypothyroid women at delivery was compared and found to have no statistically significant association, p value 0.331 (Table 4).

Table 4: Thyroid status and preeclampsia.

Thyroid status	Pre-eclampsia		Total
	Absent	Present	
Euthyroid	35 (83.3%)	7 (16.7%)	42
Hypothyroid	5 (62.5%)	3 (37.5%)	8
Total	40 (80%)	10 (20%)	50

P value 0.331.

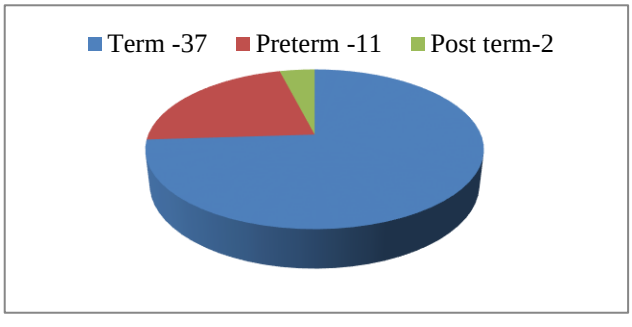

Figure 2: Gestational age at delivery n=50.

Out of these 50 subjects 37 (74%) delivered at term, 11 (22%) had preterm delivery and 2(4%)delivered post term (Figure 2). 26 (52%) women had normal vaginal delivery, 22 (44%) needed caesarean section and 2 (4%) needed assisted vaginal delivery.

Out of 50 neonates 44% had complications, low birth weight (28%), prematurity (22%), were the commonest complications (Table 5). There were 3 cases of perinatal loss (1 stillbirth and 2 neonatal deaths), all 3 in the hypothyroid women.

8 babies (20%) of the 42 euthyroid women were born prematurely, while 3 babies (37.5%) of the 8 hypothyroid women were born prematurely, which was statistically significant with p value - 0.014 (Table 6).

Table 5: Neonatal outcome.

	Number of babies n = 50	Percentage
No complications	28	56 %
Prematurity	11	22 %
Low birth weight	14	28 %
Neonatal jaundice	4	8 %
Meconium aspiration	3	6 %
Stillbirth	1	2 %
Congenital anomaly	-	-
ICU admission	6	12%
NND	2	4%

Table 6: Thyroid status and prematurity.

Thyroid status		Gestational age		Total
		> 37 weeks	< 37 weeks	
Euthyroid	Number of patients (n=42)	34	8	42
	Percentage	81%	19%	100%
Hypothyroid	Number of patients (n=8)	5	3	8
	Percentage	62.50%	37.50%	100%
Total	Number of babies	39	11	50
	Percentge	78%	22%	100%

Chi square 6.096, P value 0.014.

DISCUSSION

The prevalence of hypothyroidism was noted to be 2.54% in our obstetric population during the study period and was in accordance with other reports.[1]Where as high prevalence was reported from various parts of India.[3] The mean age of women in this study was 27.2 years (SD±4.55). 46% of women were primigravida and 54% multigravida.10% of our study population were obese and32% were over-weight. 26% of women in the study group has history of poor obstetric outcome in the form of abortions (24%), unexplained still birth (2%), 12% had taken treatment for infertility. Maternal complications were seen in the form of anaemia in 18 (36%), PIH in 13 (26%), placental abruption in 2 (4%), Placenta previa in 2(4%) and postpartum haemorrhage in 3 (6%) cases. Occurrence of preeclampsia was 37.5% in inadequately controlled thyroid status, where as it was 16.5% in adequately controlled but it was not statistically significant (P value 0.331). Various other studies have shown a significant association between hypothyroidism and gestational hypertension and preeclampsia.[17,19] There were 2 cases of abruption both occurred in patient with inadequately controlled hypothyroidism which was statistically significant (P value-0.023). Out of 3 cases of post-partum hemorrhage, 2 women had inadequately controlled hypothyroidism which was statistically significant (p value 0.014). The occurrence of pregnancy induced hypertension in this study was 26%, which is comparable to our hospital statistics (21.6%). There is two times higher incidence of abruption and placenta previa in hypothyroid patients in our study compared to our hospital statistics where abruption and placenta previa accounts for 2.1% and 1.8% respectively.

Mode of delivery in this study, the overall rate of caesarean section was 44%, which was comparable with our hospital statistics of overall CS rate (42%).[18]

But in our study 18% of caesarean section were due to fetal distress which was higher when compared with the hospital statistics which was 7% (statistically significant). Increased incidence of fetal distress was also reported by sahu et al in his study.[20] There is high incidence of fetal distress in pregnancy with hypothyroidism and it was suggested that hypothyroidism may exert irreversible effect on the fetus and placenta in early pregnancy that impair their subsequent ability to tolerate stress there by increasing the incidence of fetal distress in labour.

In this study 14 neonates (28%) had low birth weight; out of which majority were preterm babies (78%) which were statistically significant. There was one still birth at 32 weeks of gestation. None of the babies had congenital malformation. Three babies had neonatal jaundice which required phototherapy, but statistically not significant.

The overall neonatal survival rate was 94% with perinatal mortality rate of 6% which was statistically not significant. There was only one case of still birth which was due to abruptio placentae at 32 weeks. The women had hypothyroidism which was not under control. There were two cases of neonatal death, both are early preterm babies. Both had subclinical hypothyroidism not under control. In this study woman with adequately controlled hypothyroidism, neonatal outcome was 100% satisfactory.

All neonates had normal thyroid function. Thyroid function tests could not be performed in 3 babies (one case of still birth, and two cases of neonatal death).

CONCLUSION

Out of 50 subclinical hypothyroid women 84% were euthyroid and 16% had hypothyroidism which was not under control at the time of delivery. The evolution of pregnancies including maternal complications and perinatal outcome did not depend upon whether hypothyroid is subclinical or overt but mainly on the treatment received and whether the patient was euthyroid or hypothyroid at the time of delivery. 62.5% of women who were on levothyroxine prior to pregnancy needed dose increment during pregnancy to maintain euthyroid state.

There was statistically significant association between inadequately controlled hypothyroidism and maternal complications like anemia, placental abruption, placenta previa, postpartum hemorrhage, and pre-term delivery. There was also increased incidence of fetal distress in women with hypothyroidism which resulted in significant increase in caesarean section.

Regarding neonatal outcome there was statistically significant association between in adequately controlled hypothyroidism and low birth weight due to prematurity. Neo natal outcome was satisfactory in women who were adequately treated and euthyroid at the time of delivery. Hence it may be prudent to say that it is beneficial to treat all women with hypothyroidism including subclinical hypothyroidism, hence screening all pregnant women for thyroid dysfunction is recommended. Small sample size in this study maybe a limiting factor. Considering this as a pilot study, we are planning for a larger case control study based on this.

ACKNOWLEDGEMENTS

Author would like to thank the Institutional Research committee for supporting us through the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Radha KR, Sugunan N, Resmy CR. Do we need to screen and treat pregnant women for subclinical hypothyroidism? A cross sectional study in a rural tertiary centre in Kerala, India. Int J Reprod Contracept Obstet Gynecol 2017;6:781-6.