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Dr. Fathima Thasneem EA
Junior Resident, Department of Obstetrics and Gynaecology, MES Medical College Perinthalmanna, Malappuram, Kerala, India

Dr. Shahnas M
Assistant Professor, Department of Obstetrics and Gynaecology, MES Medical College, Perinthalmanna, Malappuram, Kerala, India

Dr. Abdul Vahab KP
Professor and Head, Department of Obstetrics and Gynaecology, MES Medical College, Perinthalmanna, Malappuram, Kerala, India

Corresponding Author:
Dr. Shahnas M
Assistant Professor, Department of Obstetrics and Gynaecology, MES Medical College, Perinthalmanna, Malappuram, Kerala, India

Obstetric and neonatal outcome ofthyroid dysfunction in pregnancy

Dr. Fathima Thasneem EA, Dr. Shahnas M and Dr. Abdul Vahab KP

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Abstract
Background & Objectives: Thyroid dysfunction in pregnancy and its impact on pregnancy outcome has been a topic of discussion for long and there is no consensus regarding it among experts worldwide. The aim of the study was to determine the current prevalence of thyroid dysfunction in normal pregnant women and study its impact on obstetric and neonatal outcome.
Methods: 618 pregnant women less than 16 weeks of gestation enrolled for the study. Along with routine obstetrical investigations, TSH was done. Free T3 and Free T4 estimated for patients with abnormal TSH. Patients were evaluated at the time of pregnancy termination and obstetrical and perinatal outcomes noted.
Results & Discussion: The prevalence of subclinical hypothyroidism, overt hypothyroidism and overt hyperthyroidism were 13.6%, 6% and 0.8% respectively. Maternal outcomes having significant association with overt hypothyroidism were preeclampsia (36.1% vs 11.7%), Oligohydramnios (19.4% vs 5.4%) and fetal distress in labor (19.4% vs 7.9%). Maternal outcomes having significant association with subclinical hypothyroidism were preeclampsia (26.3% vs 11.7%), placenta praevia (7.9%vs3%), dystocia (10.5%vs4.3%) and fetal distress in labour (15.8% vs 7.9%). Intra uterine growth restriction and Neonatal low birth weight also had significant association with hypothyroidism. Congenital hypothyroidism noted in 0.5% of the neonates.
Conclusion: The prevalence of thyroid dysfunction was high in our study with significant associated adverse outcomes. Hence, routine screening of thyroid dysfunction is recommended.

Keywords: thyroid dysfunction; prevalence; maternal outcome; universal screening

Introduction
Thyroid dysfunction during pregnancy had been an important area of research in clinical endocrinology and modern obstetrics due to the immense impact of subtle variations from euthyroid status on maternal as well as fetal wellbeing. There is an intimate relationship between maternal and fetal thyroid function that influences the global development of the foetus from the day of conception. Moreover, thyroid auto antibodies have been associated with increased early pregnancy wastage, and uncontrolled thyrotoxicosis and untreated hypothyroidism are both associated with adverse pregnancy outcomes beyond doubt [1, 2]. An area of continuing debate is with regard to subclinical hypothyroidism, its significant effects on pregnancy, and the decision regarding its management[1]. Finally, there is evidence that autoimmune thyroid disorder severity may be ameliorated during pregnancy, only to be exacerbated postpartum [1]. When it comes to fetal well-being, the most unanimously discussed concern is the embryo-fetal neurogenesis and psychomotor development in infants which is mostly attributed to maternal thyroid hypofunction. A study shows that hypothyroidism was found in seven (4.12%) women with recurrent pregnancy loss and one in control group [3]. Another study in Delhi concludes that there is a high prevalence of hypothyroidism (14.3%), majority being subclinical in pregnant women during first trimester from India and universal screening of hypothyroidism may be desirable in our country [4]. Further a study from Mumbai detected 4.8% prevalence of hypothyroidism and 12.4% thyroid auto immunity and concluded significant association between hypothyroidism and miscarriage [5]. Therefore are few reports of prevalence of thyroid dysfunction in pregnancy in Indian women and very few from Kerala. Also there are wide variations in the thyroid status between geographic areas and genetic pools. In this context, this study is designed to evaluate the prevalence of thyroid dysfunction in an area where iodine deficiency is more likely to come into play upon the thyroid homeostasis of females who get pregnant at an early age and more frequently.

Materials and Methods

The study included consecutive pregnant women seeking antenatal care at Department of Obstetrics and Gynaecology at MES Medical College Perinthalmanna during January - December 2016. Assuming the prevalence of hypothyroidism 14%, the sample size was calculated to be 618. Antenatal women with singleton pregnancy less than 16 weeks gestation were included. Women with already diagnosed thyroid illness, with overt diabetes, hypertension and infertility treatment were excluded. First 618 antenatal women attending the antenatal clinic meeting the inclusion and exclusion criteria were enrolled into the study after taking their written informed consent. Baseline details like age, height, weight, socioeconomic status obstetric score and baseline haemoglobin were recorded using a semi structured questionnaire. Serum TSH was assessed for all enrolled women. For women with abnormal value of serum TSH for gestation, freeT3 and freeT4 evaluated and their thyroid status defined. TSH was assayed by Eliscan kit using the principles of the sandwich ELISA. The reference range used in the study was based on guidelines of the American thyroid association 2011 for the diagnosis and management of thyroid disease during pregnancy and postpartum. Data analysis was done according to the appropriate statistical tests and statistical software. Descriptive statistics such as percentage mean and standard deviation were used to describe the parameters used in the study. Statistical package SPSS 17.0 version was used to analyze the data. Association between thyroid dysfunction and various pregnancy outcomes were studied using chi square test.

Results

The study group consisted of majority(69.6%) 20-30 years age group. 15% were teenage pregnancies, 10% were above 30 years and 5.2% were above 35 years. 60.8% of the study population were multigravidas and 29.2% were primigravidas. According to modified Kuppuswamy scale**,** 88.2% of study population belonged to lower middle class or below. There were 2% grand multigravidas. 8% of the population were mothers with bad obstetric history. The mean age was 25.8+/-4.8 years. 2.3 percent of the women were under weight and 5.7 percent were obese. Around 25% of the study population were overweight. However majority, ie, 67.3% had normal BMI. The mean BMI was 23.6%. 24.7 % of the study group were multi gravidas with previous cesarean section. 15.6 % of the pregnant women in our study had preeclampsia. 84.4 percent were normotensive.

Mild or moderate anemia was seen in 26% cases. The minimum Hb of the sample was 7g/dl. 2.4% had gestational thrombocytopenia which were all self limited. 6.5% women had hyperemesis Gravidarum while 2.5% had transient thyrotoxicosis associated with hyperemesis. 4.1% of the mothers had placenta praevia and 1.4% had abruption placenta and delivered live baby. 1.5% mothers sustained intra uterine fetal demise. The percentage of PROM was 1.2%. 9.6% mothers had oligohydramnios whereas 1.4% had polyhydramnios. The percentage of IUGR was 3.5. Oligohydramnios was the most common antenatal complication after hypertension and diabetes in pregnancy. Fetal distress was the most frequent indication for emergency cesarean section amounting to 11.4% followed by non-progression of labour which was 6.1%. 2.9 % underwent emergency cesarean section due to failed induction. 2.4% were taken for emergency LSCS due to Meconium stained Amniotic Fluid seen in labour. 2.7% mothers underwent LSCS due to breech presentation. 17 patients with previous cesarean section were taken for emergency LSCS due to scar tenderness and signs of scar dehiscence. 9 out of 21 placenta praevia had placenta accreta into previous cesarean scar. 23% of the babies in our study mothers had birth weight less than 2.5 kg.

79.3 % of the subjects were euthyroid. The most common thyroid dysfunction was subclinical hypothyroidism which was 13.6% followed by overt hypothyroidism which was 6%. There were no subclinical hyperthyroidism. 5 patients had overt hyperthyroidism. 2 patients had thyrotoxicosis associated with molar pregnancy. The percentage of preeclampsia disorder was more in hypothyroid women than euthyroid women and our results showed a highly significant association between the two variables. When the percentage of preeclampsia in euthyroid women were compared to the percentage of preeclampsia in subclinical hypothyroidism a significant association was obtained at a p value of 0.001. Also, when percentage of preeclampsia was compared among euthyroid and overt hypothyroid women, the p value was 0.000 which was again significant. (Table 1)

There was a significant association between oligohydramnios and IUGR with hypothyroidism. The p value was significant when their percentage was compared among euthyroid and overt hypothyroid subjects. There was no significant association between these variables and subclinical hypothyroidism. But, the p value was 0.044 when percentage of placenta praevia was compared among euthyroid and subclinical hypothyroid subjects which was significant. There was a significant association between non progression of labour and fetal distress with subclinical hypothyroidism whereas the association was significant only in fetal distress and overt hypothyroidism (Table 1).

On comparing the neonatal birth weight among euthyroid, subclinical hypothyroid and overt hypothyroid patients a significant association was obtained at a p value <0.01. 89% women who miscarried during our study were euthyroid. 7.4% had subclinical hypothyroidism and 0.9% had overt hypothyroidism. There was a significant association between subclinical hypothyroidism and miscarriage. (Table 1)

Table 1: Comparison of obstetric and neonatal outcome with thyroid status

Variable	Thyroid Status		$\chi 2$	p
	Euthyroid	**Subclinical Hypothyroidism**		
Eclampsia	46/346	20/56	11.17	0.001
Oligohydramnios	23/396	8/85	9.41	0.002
IUGR	10/400	4/75	7.7	0.006
Placenta praevia	12/400	6/75	4.07	0.04
Non progression	17/395	8/76	4.88	0.027
Fetal distress	31/392	12/ 76	4.81	0.028
Miscarriage	96/490	8/84	4.9	0.027
	Euthyroid	**Overt Hypoithyroidism**		
Preeclampsia	46/346	13/23	16.49	<0.001
Oligohydramnios	23/396	7/36	9.41	0.002
IUGR	10/400	4/36	7.7	0.006
Placenta praevia	12/400	3/36	2.74	0.09
Non progression	17/395	4/36	3.28	0.070
Fetal distress	31/392	7/36	3.78	0.052

Discussion

The prevalence of hyperthyroidism in our study is comparable to existing statistics across literature [4-7]. Most of the literature regarding thyroid dysfunction in pregnancy has studied the association between preeclampsia and thyroid dysfunction and majority have concluded significant association between sub clinical hypothyroidism and preeclampsia. In our study we have got a p value 0.001 which means significant association between

subclinical hypothyroidism and preeclampsia. A previous study also showed a significant association between subclinical hypothyroidism and preeclampsia but not with overt hypothyroidism [5]. In our study the prevalence of overt hypothyroidism was slightly higher and the sample relatively small. Also, our sample had more of overweight and obese women which indeed is a known risk factor for preeclampsia. In the present study a significant association was obtained between overt hypothyroidism and IUGR-Oligohydramnios with a p value significant at 0.01 level. An earlier study also had similar findings with an association between overt hypothyroidism and IUGR. This may be understood in the light of association between preeclampsia and hypothyroidism [7]. In our study spontaneous preterm births were 3.5% of the sample and 44% of them had hypothyroidism. The number of preterm births was less (18) and too small to comment on the significant association. Preterm birth was a significant association in both subclinical as well as overt hypothyroidism in study conducted by in India. In our study we got a significant association between subclinical hypothyroidism and placenta praevia with a p value of 0.04. The association has not been seen in earlier studies and needs further research to generalize this finding [8].

In the present study dystocia and fetal distress was having significant association with subclinical hypothyroidism. However previous studies are contardictory and one showed no asssociation between fetal distress or dystocia with thyroid status, while another study from India found significant association between fetal distress and overt hypothyroidism [9]. So this finding also needs further research. Our study found that 8% of the abortions had hypothyroidism. A study showed that untreated hypothyroidism, subclinical, or overt, at the time of conception is associated with miscarriage rate of 31.4% compared with 4% in euthyroid subjects at conception. Another study concluded a high rate of miscarriage in pregnant women with thyroid auto immunity [10]. In our study we could find a significant association between subclinical hypothyroidism and miscarriage.

Hence, the data in present study gives a high prevalence of thyroid dysfunction and significant associations between hypothyroidism and pregnancy complications in subjects attending a tertiary care centre catering to predominantly lower middle class population. Therefore more stringent routine screening for hypothyroidism is needed, especially in India, and larger randomised control trials need to be done to support this fact and to know whether treatment with thyroxine in subclinical hypothyroidism improves pregnancy outcome.

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