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Original Article

Obstetrics and Gynaecology Section

Feto-maternal Outcome Using New Screening Criteria of Serum TSH for Diagnosing Hypothyroidism in Pregnancy

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ABSTRACT

Introduction: Evidence suggests that by using the classical non pregnant reference range for serum TSH (STSH), one might miss hypothyroidism in pregnancy. Therefore, upper normal cut off value of S TSH should be taken as <2.5 mIU/L in the first trimester and <3mIU/L in the second and third trimester. However, two Indian studies have reported higher trimester specific reference ranges in the Indian pregnant women.

Objectives: To assess the maternal and fetal outcomes using new screening criteria with upper S TSH cut off as >3mIU/L, for diagnosing hypothyroidism in pregnancy.

Materials and Methods: This study was a cross sectional study, carried out in the Department of Obstetrics and Gynaecology of a tertiary care hospital, in collaboration with the Department of Endocrinology. Pregnant women with ≤ 20 weeks gestation, attending antenatal OPD from December 2010 to January 2012 were included in the study. On the basis of S TSH level, women were divided into Study Group with S TSH level between 3.1 to 6.2 mIU/L, (new range to be studied) and an equal number of age and parity matched Control Group with S TSH levels between 0.4 to 3 mIU/L. The maternal and fetal outcomes were compared between study and control groups.

Results: During the study period, a total of 66 women had S TSH between 3.1-6.2 mIU/L. Maternal and fetal outcomes in both the groups were comparable. There was no difference in the mode of delivery between study and control groups.

Conclusion: The lower S TSH cut off recommended for diagnosing hypothyroidism in pregnancy may not be applicable to pregnant Indian women.

Keywords: Endocrinological disorders, Reference values, Screening in pregnancy, Serum TSH

INTRODUCTION

Thyroid disorders are the commonest endocrinological disorders encountered in pregnancy [1]. The reported prevalence of hypothyroidism varies from 0.3 to 11.1%, with subclinical hypothyroidism (SCH) being more frequently encountered than overt hypothyroidism (OH) [2-10]. Despite being common, thyroid disorders are often overlooked because of the nonspecific nature of symptoms and hypermetabolic state of pregnancy [1]. Hence estimation of Serum Thyroxine Stimulating Hormone (S TSH) plays a pivotal role in the evaluation of maternal thyroid status [11].

Optimum maternal thyroid function during pregnancy is important for both the mother and the fetus. During the first trimester, fetus is dependent on the mother for the thyroid hormones that are required for its optimal growth and development. Maternal hypothyroidism has also been associated with adverse pregnancy complications, including abortion, preterm birth and placental abruption [5,9,12-15].

The profound physiological changes of pregnancy significantly affect the interpretation of thyroid function. Consequently, thyroid function test results of healthy pregnant women differ from those of healthy non pregnant women. As such, the criteria for diagnosing hypothyroidism on the basis of S TSH during pregnancy have been changing. Although S TSH values of 4.0-6.0 mIU/L were considered normal in the past, recent opinions suggest that first trimester values >2.5 mIU/L and second and third trimester values >3mIU/L are associated with adverse fetomaternal outcome [4,9,11,12]. There is increasing evidence that by using the classical non pregnant reference range, one might misdiagnose those women as euthyroid who actually have a slight S TSH elevation [11]. American Thyroid Association (ATA) Guidelines also recommend that for women on L-thyroxine therapy, S TSH should be aimed at <2.5 mIU/L in the first trimester and <3.0 mIU/L in the second and third trimester [16]. However, two Indian studies have reported higher trimester specific reference ranges in the Indian pregnant women [8,17]. Despite these conflicting observations, Indian researchers have reported improvement in the fetomaternal outcomes when pregnant women with S TSH >3mIU/L were considered hypothyroid and received treatment with L Thyroxine [18].

Keeping this point in view, the present study was planned to assess the maternal and fetal outcomes using new screening criteria with upper S TSH cut off as >3mIU/L, for diagnosing hypothyroidism in pregnancy.

MATERIALS AND METHODS

This study was a cross-sectional study, carried out in the Department of Obstetrics and Gynaecology of a tertiary care hospital, in collaboration with the Department of Endocrinology. Pregnant women with ≤ 20 wk gestation, attending antenatal OPD from December 2010 to January 2012, planning to deliver at this institute and willing to comply with the study protocol were enrolled in the study. Women with chronic medical disorders, known thyroid disorder, bad obstetrics history with a known cause and multiple pregnancies were excluded from the study. Along with routine antenatal investigations, Serum thyroid stimulating hormone (S TSH) assay was done by ELISA technique. On the basis of S TSH level, women were divided into Study Group with S TSH level between 3.1 to 6.2 mIU/L (new range to be studied) and an equal number of age and parity matched Control Group with S TSH levels between 0.4 to 3 mIU/L (institution's laboratory non pregnant reference range of S TSH is 0.4-6.2 mIU/L). Women with S TSH between 3.1 to 6.2 mIU/L were tested for S FT4 by ELISA technique and the reference range of 0.76-2.24 ng/dl was taken as normal. After obtaining informed consent, a detailed history and examination was done; women in

study group were referred to the endocrinologist but treatment was not initiated. The women were followed till delivery as per the routine hospital protocol. The maternal outcomes compared between study and control groups were spontaneous abortion, gestational hypertension, preeclampsia, gestational diabetes mellitus and mode of delivery. The fetal outcome studied were prematurity, intrauterine growth restriction, fetal distress, intrauterine fetal death, low apgar at 5 minutes, and neonatal ICU admission.

STATISTICAL ANALYSIS

Data was analyzed using Pearson Chi-square test. The significance level was set at $p<0.05$. Statistical analysis was performed with SPSS 12.0 for windows.

RESULTS

A total of 66 women with S TSH between 3.1-6.2 mIU/L were enrolled in the study group. Equal number of age and parity matched women were included in the control group. The mean age of women in study and control groups was 23.9±3.1 and 24±3.1 y, respectively. Majority of women in both groups had normal BMI, 72.72% in study and 53.03% in the control group. The S FT4 of all the women in the study group was within the normal reference range. The maternal and fetal outcomes and mode of delivery in both the groups were comparable [Table/Fig-1-3].

Maternal variables	Study Group (n=66)		Control Group (n=66)		p value
	Number	Percent	Number	Percent	
Spontaneous abortion	1	1.51	1	1.51	1
GHTN*	0	0	2	3.03	0.154
PE**	2	3.03	1	1.51	0.559
GDM***	4	6.06	1	1.51	0.171
Placental abruption	0	-	0	-	-

[Table/Fig-1]: Maternal outcome in the study and control groups
*gestational hypertension, **preeclampsia, ***gestational diabetes mellitus

Fetal variables	Study Group (n=66)		Control Group (n=66)		p value
	Number	Percent	Number	Percent	
Prematurity	2	3.03	1	1.51	0.55
IUGR*	7	10.60	5	7.57	0.54
FD**	10	15.15	8	12.12	0.4
IUFD***	2	3.03	0	-	0.154
Low APGAR at 5 minutes	4	6.06	1	1.51	0.171
NICU**** admission	5	7	2	3	0.30

[Table/Fig-2]: Fetal outcomes in the study and control groups
*intrauterine growth restriction, **fetal distress, ***intrauterine fetal death, ****neonatal ICU

Mode of delivery	Study group (n=65)*		Control group (n=65)*		p value
	Number	Percentage	Number	Percentage	
Vaginal delivery	56	86.15	59	90.76	0.310
caesarean for fetal distress	4	6.15	4	6.15	1
Caesarean for other causes	5	7.69	2	3.07	0.244

[Table/Fig-3]: Distribution of women according to mode of delivery
*n=65 as one women in each group aborted

DISCUSSION

As per the latest ATA guidelines, gestation specific reference ranges should be used for interpretation of the thyroid function and when trimester specific S TSH reference ranges are not available, the following cut offs may be used: first trimester, <2.5 mIU/L; second trimester, <3 mIU/L; third trimester, <3 mIU/L [15].

The present study did not find any difference in the rate of spontaneous abortion between women in study and control group, p=1.00. Similar results from Indian population are reported by Nambiar et al., who also reported similar rate of miscarriage in thyroid autoimmune negative women with S TSH between 0.1 to 2 and between 2 to 4 mIU/L, i.e. 7.35% and 7.5%, respectively [10]. However, our findings are in contrast to the observation by Negro et al., who reported increased pregnancy loss in women with S TSH between 2.5 and 5.0 mIU/L in the first trimester of pregnancy [12].

Other maternal complications like Preeclampsia, gestational diabetes and placental abruption were also similar in the study and control group. There have been reports of increased incidence of preeclampsia with overt and subclinical hypothyroidism [14,19,20], however, other studies failed to demonstrate such association [6,9,14,19,20]. Aziz et al., reported high incidence of gestational diabetes mellitus (GDM) in hypothyroid women; however their study was not case controlled [7]. Cleary Goldman did not find any association between GDM and subclinical hypothyroidism (SCH) [6]. The mode of delivery and caesarean section for foetal distress were comparable in both study and control group. However, Sahu et al., have reported higher number of caesarean section for fetal distress in women with SCH [9]. The studies by Nambiar et al., and Negro et al., did not comment on these outcomes [10,12].

In the present study, the risk of preterm birth was not increased in the women with new S TSH criteria range as compared to controls. In a previous study, Casey et al., have reported 2 fold risk of preterm birth at ≤34 wk in women with SCH as compared to control, whereas, Negro et al., did not observe increase in preterm or very preterm birth in women with S TSH between 2.5- 5 as compared to those with TSH <2.5 mIU/L. [5,12] Similarly, Nambiar et al., also observed comparable rates of preterm delivery in thyroid autoimmune negative women with S TSH between 0.1 to 2 and 2 to 4 mIU/L, 5.14% and 10%, respectively [10].

None of the studies, including the present study, testing lower reference range of S TSH, observed any association of S TSH levels with the occurrence of still births [10,12]. The incidence of fetal distress, low APGAR score at 5 minutes and NICU admission in the present study was comparable in both the groups.

Studies from countries like USA, China and Switzerland have established trimester specific reference ranges for S TSH during pregnancy which were found to be lower than their non-pregnant counterparts [21-23]. The present study was designed to assess this lower threshold and effect of S TSH >3mIU/L on feto-maternal outcome by applying the lower S TSH threshold in Indian population; however no statistically significant difference in the maternal and fetal outcome was observed in this group as compared with controls.

In India, the trimester specific S. TSH reference ranges have been reported by Kumar et al., and Marwaha et al., and are shown to be higher than that of reports from Western literature [8,17]. In the study by Kumar et al., it was suggested that due to reduced availability of Iodine the S TSH during pregnancy in Indian women is high and significantly overlaps with that of non pregnant state [17]. Similarly, Marwaha et al., established the trimester specific reference range for S TSH using 5th and 95th percentile, as 0.6-5.0, 0.44-5.78 and 0.74-5.7 mIU/L, in the first, second and third trimester of pregnancy, respectively; these values are higher than those reported by other countries.

CONCLUSION

Women with S TSH levels between 3.1-6.2mIU/L are at no added risk of adverse fetomaternal outcome as compared to women with S TSH levels <3mIU/L. Hence, the lower S TSH cut off recommended for diagnosing hypothyroidism in pregnancy may not be applicable to pregnant Indian women.

The major limitation of this study was its small sample size and hospital based population.

Ethical clearance: Ethical clearance was taken from ethical committee of the institution

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