International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 1 (2014) No.1, pp. 112-121
http://www.ijogr.com/

Subclinical Hypothyroidism and Its Effect on Pregnancy Outcome

[1]Rupali M , Dilip K. B, Santanu B, Amitava P, Tapan K. M

[1]Department of Obstetrics and Gynaecology, R.G.Kar Medical College, Kolkata, India

Department of Obstetrics and Gynaecology, Burdwan Medical College, Burdwan, India

Email: rupali.628@rediffmail.com,santanu82.doc@gmail.com,drdkb75@gmail.com
amitava.628@rediffmail.com,tapanobsmandal@gmail.com

Abstract

A prospective analytical study was done on Eight hundred sixty nine antenatal women with singleton pregnancy at 36-38 weeks of gestation. Apart from history taking and examination maternal serum TSH and FT4 were measured. Thirty five subclinical hypothyroid mothers were noted and they were compared with 105 euthyroid pregnant women as control matched to the case in relation to age parity and ethnicity. Mother was followed up till discharge from hospital. Newborn weight, Apgar score and serum TSH after 48 hours of birth to 7 days was measured. Maternal obstetrical and perinatal outcomes were noted. The prevalence of subclinical hypothyroidism was 4.38%. Adverse maternal outcome in subclinical hypothyroidism was associated with preeclampsia (17.14 vs. 1.90%), placental abruption (8.57 vs. 0.95%) as compared to euthyroid pregnant women. Adverse fetal outcome in subclinical hypothyroidism includes LBW (33.33 vs. 26.67%), IUGR (14.29 vs.0.95), still born (14.29 vs. 0.00%), jaundice (13.33 vs. 1.90%), and RDS (10.00 vs. 0.95%) as opposed to euthyroid women. Subclinical hypothyroidism associated with pregnancy can result in poor obstetric outcome and neonatal complications occur more frequently.

Keywords

Serum TSH, FT4, prevalence, maternal outcome, fetal outcome

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I. Introduction

Pregnancy is associated with significant modification of thyroid function. The physiological changes in pregnancy are mainly due to increased level of thyroid binding globulin (TBG) by marked elevation of estrogen and human chorionic gonadotropin, increased renal blood flow and glomarular filtration rate leading to increased iodide clearance from plasma which causes decreased thyroid hormone release resulting in some degree of organ hypertrophy induced by excess TSH[1]. Thyroid function disorder can affect both present as well as future pregnancy. The prevalence of subclinical hypothyroidism complicating pregnancy has been reported to range from 2-3% of women [2]. Subclinical hypothyroidism is a condition that exhibits an elevated TSH level and normal level of serum thyroxin [3]. Subclinical hypothyroidism remains frequently unrecognised unless screening programme are initiated during early pregnancy. Women with overt and subclinical hypothyroidism may be associated with poor pregnancy outcome such as preeclampsia, placental abruption, preterm labor, low birth weight babies, intrauterine growth restriction, still birth, higher incidence of neonatal hypothyroidism and increased perinatal mortality [4].

The present study was conducted to find out the prevalence of subclinical thyroid dysfunction in pregnancy and also to evaluate maternal and fetal outcome.

II. Materials and Methods

The prospective observation analytical study was conducted in Burdwan Medical College and Hospital, Burdwan, West Bengal, India over April 2012 to March 2013. The study was approved by the medical ethics committee of the institution according to revised Helsinki 2000 protocol. A total of eight hundred sixty nine antenatal mothers were enrolled from outpatient department of Gynecology &Obstetrics. Thirty five subclinical hypothyroidism (SCH) cases were detected from assigned pregnant mothers. Other 105 antenatal mothers were selected as control matched by same age (±2 years) and parity giving rise case to control ratio of 1:3. Comparisons have been done between 35 sub clinical hypothyroid cases to 105 euthyroid control for data analysis. *Inclusion criteria* included in the study were young (15-30 yrs ; P_{0+2}) healthy women with singleton fetus at 36- 38 weeks of gestation without labor pain. Certain high risk factors like multi-fetal pregnancy, symptoms suggestive of thyroid dysfunction, autoimmune disorders and diabetes mellitus were excluded from our study. After taking informed consent from the patient the detailed history was elicited followed by general, systemic and obstetrical examinations regarding presentation, position, gestation age, amount of liquor and routine investigations including thyroid profile was done. The gestational age was based on the woman's first day of last menstrual period (LMP), with sonography performed if there were discrepancies between fundal height and LMP or if the LMP was uncertain.

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Sample size

Eight hundred sixty nine antenatal mothers having singleton pregnancy at 36-38 weeks were assessed for eligibility for inclusion in the study in the *'reference period'* of one year. Sixty nine cases were excluded either due to not meeting the inclusion criteria (n=60) or due to refusal of enrolment (n=9). Finally 800 antenatal mothers were studied in details and thirty five antenatal mothers have been diagnosed to have subclinical hypothyroidism. Out of 765 euthroid (ETH) antenatal mothers, 65 mothers did not attended OPD for follow-up during the course of study or come for delivery and have been excluded from data analysis. Finally critical statistical analysis and comparisons were made on 35 SCH and 105 ETH cases, resulting 1:3 ratios **[Figure 1]**

Assessments

Apart from history –taking and clinical examinations, routine investigations and examination of new born was done immediately after birth to note body weight, Apgar score and any congenital anomaly. All the new born babies and mothers were followed up till discharge from hospital.

Thyroid parameters

Maternal serum TSH and FT_4 level were measured at 36-38 weeks of gestational age. Serum TSH was measured using a solid-phase, two-site chemiluminescent enzyme immunometric assay. Serum FT_4 concentration was also measured by means of a solid-phase immunometric assay. Euthyroid (ETH) was defined as normal TSH (0.2-3.0 miu/l). Subclinical hypothyroid, defined as TSH (>3 miu/l) in the presence of normal level of free T_4 (0.8-2ng/dl) [6].

New born TSH was measured after 48 hours to 7 days following delivery .Blood collected in filter paper and measured by Flurometric assay. When the level of TSH is ≥20 mIU/l, treatment was given.

Other parameters

Height and weight of antenatal mothers were measured and BMI was calculated. BMI = Weight in kilogram/ height in meter^2.Preeclampsia is defined as persistent rise of BP ≥140/90 after 20 weeks of pregnancy on more than two occasions with proteinuria. Anemia was considered when the value of hemoglobin in the peripheral blood was ≤ 10gm%. Intrauterine growth restriction was considered when birth weight was less than 10th percentile for gestational age. LBW was defined as weight ≤2500gm. Low Apgar Score was considered when Apgar score was below 7 at 1 minute. Still birth is defined as death of fetus at or after 28 weeks of gestation or at the time of birth. Early neonatal death is the death of neonates within 7 days of birth.

Define other parameters as well as mentioned in the tables 2-4.

Statistical analysis was performed by using software package of Stat Calc version 7.1.1.and Epi Info 3.3.2. Calculation of mean, standard deviation and odds ratio (OR) with 95% confidence interval (CI) was done. Student's t-test and chi- square analysis and Fisher's exact test were done to assess the significance of difference in the risk between groups and p- value less than 0.05 is considered as significant.

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III. Results

Patients in both the groups were comparable in relation to age, body mass index, haemoglobin concentrations and mode of delivery. The mean BMI was 22.37±2.42 for euthyroid patients, and 22.85±2.32 for subclinical hypothyroid. No significant difference was noted with respect to parity and haemoglobin levels in two different groups. (**Table1**).

Subclinical hypothyroidism was significantly associated with preeclampsia (17.14 vs. 1.9%; p=0.0032), abruptio placente (8.57 vs. 0.95%, p=0.0483) and IUGR (14.29 vs. 0.95%) as compared to euthyroid mothers. No significant increased incidence of anemia was noted in subclinical hypothyroid pregnant mothers (**Table 2)**

Mothers having SCH has significant association of sepsis (14.29 vs. 0.95%), wound dehiscence (17.14 vs. 1.90%, p=0.0032) and still birth (14.29 vs. 0%, p=0.0007) as compared to euthyroid pregnant mothers (**Table 3)**

Adverse fetal out come in subclinical hypothyroidism included RDS (10.00 vs. 0.95%), jaundice (13.33 vs.1.90%), sepsis (13.33 vs. 0.95%) and NICU admission (26.67 vs. 3.81%) as compared to euthyroid women. All are statistically significant. Majority of the babies (66.67%) had birth weight more than 2.5 kg in SCH mothers, but only 33.33% had birth weight below 2.5kg, which was not statistically significant (p=0.462)(**Table 4)**. The mean birth weight between euthyroid and subclinical hypothyroid was not statistically significant (2.64±0.56 vs. 2.59±0.82 kg; p=0.759)

Figure 2 represents the box plots of 25th to 75th percentile value of TSH in two groups. In subclinical hypothyroidism the percentile value of above level ranges from 5.23 to 6.53mIU/l (Mean ±SD, 5.869±0.436 mIU/l and median value is 5.875 mIU/l) whereas the values in ETU ranges from 1.5-2.86 mIU/l (Mean ±SD, 2.178±0.422mIU/ml and median 2.3mIU/l) and the difference is statistically significant (p=0.0001)

IV. Discussion

Thyroid dysfunction is a common disorder which poses special problem during pregnancy and developing fetus. Thyroid hormone screening is very much important before pregnancy or during early trimester of pregnancy as thyroid hormone levels have important role for neurophysiologic development of baby.

In our study the prevalence rate of subclinical hypothyroidism in pregnancy is 4.38% and TSH level ≥ 6mIUl was 2.13 %(17/800). The prevalence of subclinical hypothyroidism by Casey et. al., was 2.3% in pregnant women [5], but in another study of Indian pregnant population a higher prevalence rate of 9% was noted [6].

In the present study it was found that the mean age of subclinical hypothyroid women was 25.2±3.22 years but there was no correlation of prevalence of subclinical hypothyroidism with age. Ajmani and associates[6] in their study showed that increased maternal age has higher incidence of thyroid dysfunction and the increase in prevalence of overt hypothyroidism is higher in older age group (27.16±5.237 years) due to current trend of older women becoming pregnant , but maternal age of subclinical hypothyroidism

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was 24.51±4.71 years, which corresponds with our report.

The present study had several complications in pregnancy. Preeclampsia, placental abruption, oligoamnios and IUGR were more commonly associated with subclinical hypothyroidism than euthyroid pregnant mothers. The occurrence of maternal anemia was not statistically significant in subclinical hypothyroid women when comparison was done in two groups. Casey et al found that the incidence of gestational hypertension and severe preeclampsia were similar between SCH and ETH groups, but pregnancy with subclinical hypothyroidism had three times more accidental hemorrhage [5]. From world literatures it is evident that oligoamnios has no correlation with subclinical hypothyroidism. Maternal subclinical hypothyroidism with increased rate of fetal distress in our study is in agreement with the study of Goel et. al., [7]. Hypothyroidism in early pregnancy may exert irreversible effects on fetus and placenta which impair the tolerability of stress and causes fetal distress in labor, which in turn impair the neurophysiologic development of fetus [6]. In our study stillbirth was 14.3- fold greater in subclinical hypothyroidism in comparison to euthyroid group (p=0.0007), but more (17.65 %; 3/17) stillbirth occurred at the TSH level of greater than 6mIU/l and less (11.11%; 2/18) below 6mIU/l in SCH groups [odds ratio 1.59, 95% CI 0.18-15.88, p=0.5000]. Allen and colleagues [8] reported the rate of fetal death was significantly higher in pregnancies with TSH measurement at or above 6mIU/l.

Thyroid hormone is necessary for normal placental development .Specifically, there is evidence that preterm delivery and vascular diseases such as preeclampsia and placental abruption may be causally linked to faulty early placentation [9] [10]. In the present study, no cases of congenital malformation of baby were noted. Preterm birth is one of the important causes of neurophysiologic dysfunction of children [11]. So, preterm delivery and thyroxin deficiency may potentiate the neurodevelopment abnormalities of babies in our country, though in our study no case of preterm birth was noted in subclinical hypothyroid mothers.

The limitations of our study were that TPO antibody detection was not done due to lack of funding; the duration of the study was very short, long term follow-up of babies to observe neurological complications were not possible and placental histopathological examination was not done to find out any pathological correlation.

V. Conclusion

In conclusion, the current study shows that subclinical hypothyroidism is a common disease associated with pregnancy and remains asymptomatic but can result in poor obstetric outcome.

Universal screening of subclinical hypothyroidism in pregnancy is desirable in our country to prevent adverse maternal and fetal outcome.

VI. References

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Table 1 Obstetric variables

Parameters	ETH (n=105)	SCH (n=35)	p-value
Age (Mean ±SD) years	25.3±3.32	25.2±3.22	0.876
Parity: Primi	67	19	0.316
Multi	38	16	
BMI [kg/m^2] (Mean ±SD)	22.37±2.42	22.85±2.32	0.298
Haemoglobin (Mean ±SD) gm/dl	10.69±0.72	10.78±0.63	0.483
Delivery:			
VD	60(57.14)	17(48.57)	0.377
LSCS	45(42.86)	18(51.43)	

n (%); VD, vaginal delivery; LSCS, lower segment caesarean section

Table 2 Complications of mother during antepartum period

Complications	ETH (n=105)	SCH (n=35)	Odds ratio (95% CI)	p-value*
Pre-eclampsia	2(1.90)	6(17.14)	0.09(0.01 to 0.57)	0.0032
Eclampsia	2(1.90)	2(5.71)	0.32(0.02 to 4.62)	0.2602
Anemia	3(2.86)	2(5.71)	0.49(0.05 to 6.08)	0.3672
Oligoamnios	2(1.90)	4(11.43)	0.15(0.01 to 1.13)	0.0343
Placental abruption	1(0.95)	3(8.57)	0.10(0.00 to 1.35)	0.0482
IUGR	1(0.95)	5((14.29))	0.06(0.00 to 0.56)	0.0038

* Fisher-exact test (1-tailed); n (%); IUGR, intra-uterine growth restriction

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Table 3 Distribution of patients according to postpartum complications

Complications	ETH (n=105)	SCH (n=35)	Odds ratio (95% CI)	p-value*
PPH	5(4.76)	2(5.71)	0.82(0.13 to 9.06)	0.5596
Sub-involution	1(0.95)	1(2.86)	0.33(0.00 to 26.41)	0.4388
Sepsis	1(0.95)	5(14.29)	0.06(0.00 to 0.56)	0.0038
Wound dehiscence	2(1.90)	6(17.14)	0.09(0.01 to 0.57)	0.0032
Stillbirth	0(0.00)	5(14.29)	0.00(0.00 to 0.34)	0.0007

* Fisher exact test (1-tailed); n (%), PPH, post partum hemorrhage;

Table 4 Neonatal outcome

Outcome	ETH (n=105)*	SCH (n=30)*	Odds ratio (95% CI)	p-value**
LBW (<2500gm)	28(26.67)	10(33.33)	0.73(0.28 to 1.97)	0.4739
RDS	1(0.95)	3(10.00)	0.09(0.00 to 1.15)	0.0343
Jaundice	2(1.90)	4(13.33)	0.13(0.01 to 0.95)	0.0219
Sepsis	1(0.95)	4(13.33)	0.06(0.00 to 0.68)	0.0087
NICU admission	4(3.81)	8((26.67)	0.11(0.02 to 0.46)	0.0007
Early neonatal death	2(1.90)	1(3.33)	0.56(0.03 to 34.36)	0.5325

* Only the live births in each group are included, ** Fisher exact test (1-tailed) except p-value of LBW; n (%), RDS, respiratory distress syndrome; NICU, neonatal intensive care unit

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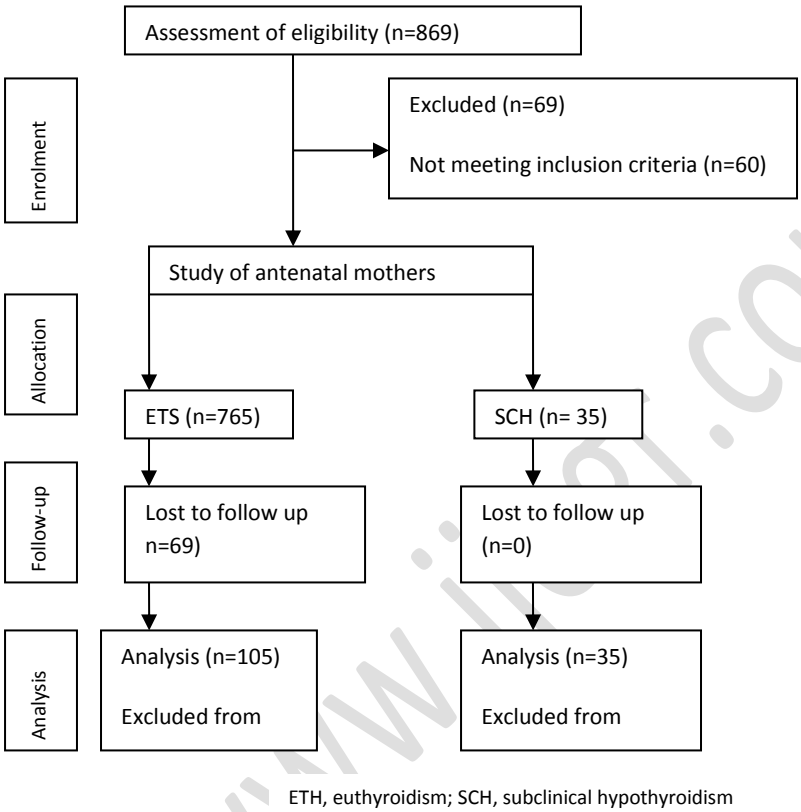

Figure 1 Patients follow through chart

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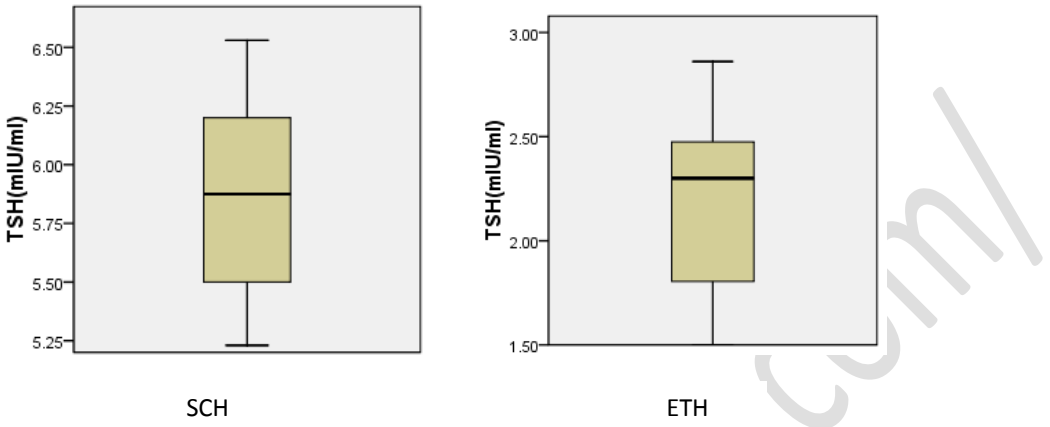

Figure2. Boxes represent 25th to 75th percentile values of TSH in subclinical hypothyroid (SCH, n=18, out of 35) and euthyroid (ETH, n=55, out of 105) pregnant mothers