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Study of Feto-Maternal Outcome in Pregnancy with Subclinical Hypothyroidism

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ABSTRACT

Background: *Hypothyroidism has a great impact on pregnancy. But there is a controversy about the maternal and perinatal outcomes of subclinical hypothyroidism (SCH). This study was placed to know the significant effects.*

Methods and Materials: *A descriptive longitudinal study was held in Z. H. Sikder Women's Medical College & Hospital, Dhaka, Bangladesh. 400 pregnant women were included in this study with purposive sampling. All antenatal patients from booking visit at 1st trimester to delivery were monitored by serum TSH and serum FT_4 levels in each trimester and fetal outcomes were also monitored 200 pregnant women were diagnosed as subclinical hypothyroidism (SCH) with random screening of initial thyroid function tests. Another 200 pregnant women were euthyroid. The study period was 3 years, from January 2020 to December 2022. To evaluate the thyroid status, maternal serum samples were collected in each trimester, total three times. Maternal outcomes, which we studied, were gestational hypertension, gestational diabetes mellitus, maternal anemia, antepartum hemorrhage, postpartum hemorrhage, placental abruption, preterm delivery, premature rupture of membranes (PROM), caesarean deliveries; perinatal outcomes were low birth weight (LBW), intrauterine growth restriction (IUGR), low Apgar score, stillbirth, congenital anomaly and NICU admission.*

Result: *This study includes 400 pregnant women, among which 200 were euthyroid and 200 were with SCH. The mean age was 27.12 ± 0.05 years in pregnancy with euthyroid group and 26.31 ± 0.25 in pregnancy with SCH group. Among the pregnancy with euthyroid group, 141 women were nullipara and 59 women were nullipara. Among the pregnancy with SCH group, 87 women were nullipara and 113 women were nullipara. Serum TSH level was 4.44 ± 0.11 in 1st trimester, 4.74 ± 0.19 in 2nd trimester, 5.45 ± 0.17 in 3rd trimester. Serum free T_4 level was 8.29 ± 0.13 in 1st trimester, 6.65 ± 0.15 in 2nd trimester, 6.67 ± 0.34 in 3rd trimester. In pregnancy with SCH group gestational hypertension, miscarriage, placental abruption and premature rupture of membranes (PROM) were significantly higher ($p<0.001$). Antepartum hemorrhage (APH), preterm delivery and Caesarian deliveries were also higher in this group ($p<0.05$). Among the neonatal outcomes, low birth weight and intrauterine growth restriction (IUGR) babies were more born in pregnancy with SCH group. Anti TPO antibody titer was significantly higher in pregnant women with SCH.*

Conclusion: *Subclinical hypothyroidism (SCH) is associated with increased risk of gestational hypertension, premature rupture of membranes (PROM), abruptio placentae and fetuses have more risk of IUGR and LBW. Therefore, routine maternal thyroid function test should be done to protect from adverse maternal and fetal outcome.*

Keywords
Subclinical hypothyroidism, Maternal outcome, Fetal outcome.

Introduction

Lots of physiological changes occur in each pregnancy including endocrine glands in order to meet the fetal and increased maternal requirements [1]. Thyroid hormones have crucial effects on pregnancy [2]. Due to two main hormones of pregnancy, human chorionic gonadotropin (hCG) and estrogen, many changes occur in thyroid hormone level during pregnancy [3]. Thyroid hormone is released with the stimulation of thyroid stimulating hormone (TSH) [4]. It has profound role in neurocognitive development of fetus and any type of deficiency in mother may results into neurocognitive impairment of the fetus [5]. Maternal hypothyroidism in early pregnancy may develop low intelligence quotient score, cognitive delay and impairment in psychomotor development in babies [6]. Hypothyroidism may not be detected as many patients are asymptomatic [7]. It may be overt or subclinical. Subclinical hypothyroidism (SCH) is a phenomenon in which serum free T_4 (FT_4) and serum free T_3 (FT_3) are normal, but serum TSH is high [8]. SCH in pregnancy was ignored before. But now-a-days it is recognized that SCH plays a significant role in pregnancy outcomes and complications may also arise as a result of this, i.e.; gestational diabetes mellitus (GDM), pre-eclampsia [9]. These women have two times higher chances to develop preterm labor and delivery of premature baby than the normal population [10]. They have also three times higher chances of abruptio placentae [11]. Different types of miscarriages also happened to these women [12].

The recent ATA (American Thyroid Association) guidelines in 2017 have recommended that, TSH concentration in a pregnant woman above 2.5mIU/L, will need evaluation of anti TPO antibody [13]. The cutoff point of S. TSH is 2.5 mIU/L in 1st trimester and 3.0 mIU/L in 2nd and 3rd trimester. They have also advised for levothyroxine supplementation for SCH in pregnancy and women with raised anti TPO antibodies [14,15].

There is lack of data in our country. Though SCH is associated with lots of complications in both mother and fetus, yet it is not routinely practiced in antenatal care booking investigations [16]. This study aims at detecting the feto-maternal outcome in pregnant women with subclinical hypothyroidism.

Methods and Materials

A descriptive longitudinal study was held in Z. H. Sikder Women's Medical College & Hospital, Dhaka, Bangladesh. 400 pregnant ladies were included in this study with purposive sampling, who attended the antenatal clinic. Among which 200 were euthyroid and 200 were diagnosed as subclinical hypothyroidism with random screening of initial thyroid function tests. The study period was 3 years, from January 2020 to December 2022. To evaluate the thyroid status, maternal serum sample were collected in each trimester. Maternal outcomes, which we studied, were gestational hypertension, gestational diabetes mellitus, maternal anemia, antepartum hemorrhage, postpartum hemorrhage, placental abruption, preterm delivery, premature rupture of membranes (PROM), caesarean deliveries; perinatal outcomes were low birth weight (LBW), intrauterine growth restriction (IUGR), low Apgar score, stillbirth, congenital anomaly.

Blood samples were taken who fulfilled the inclusion criteria. Thyroid hormones were measured by electrochemiluminescence method. Pregnant women with TSH level 2.5 to 10 mIU/L and FT_4 according to trimester specific level were considered as a case of subclinical hypothyroidism according to American Thyroid Association (ATA).

Inclusion Criteria

Singleton pregnancy.
No medical disease other than thyroid.
Willing for regular antenatal check up.

Exclusion criteria

Connective tissue diseases.

Statistical analysis

Data was analyzed in SPSS version 22. $p \leq 0.05$ was considered as significant. Prevalence was expressed in percentage and 95% CI.

Ethical clearance

All the ethical issues regarding medical research on human were discussed according to WMA declaration of Helsinki, revised in 2013. After explaining the whole procedure, patient's informed written consents were taken. Ethical clearance was obtained from Ethical committee of Z. H. Sikder women's medical college & hospital.

Result

This study includes 400 pregnant women, among which 200 were euthyroid and 200 were with SCH.

Table 1: Demographic pictures of the study population.

Variables	Pregnancy with euthyroid(n=200)	Pregnancy with SCH (n=200)	P value
Age (years)	27.12 ± 5.55	26.31 ± 6.75	0.241
Parity			
Nullipara	141	87	0.756
Multipara	59	113	0.663

In Table 1 the different demographic pictures of the study population have been shown.

Table 2: S.TSH and S. FT_4 concentrations according to trimester.

Trimester	S. TSH (mIU/L)	S. FT_4 (mIU/L)
1st	4.44 ± 0.11	8.29 ± 0.13
2nd	4.74 ± 0.19	6.65 ± 0.15
3rd	5.45 ± 0.17	6.67 ± 0.34

In Table 2 the levels of thyroid hormones in three trimesters are shown.

Table 3: Maternal factors associated with SCH.

Variables	Pregnancy with euthyroid (n=200)	Pregnancy with SCH (n=200)	P value
Gestational hypertension	32(16%)	144(72%)	<0.001
Gestational diabetes mellitus	26(13%)	31(15.5%)	0.113
Miscarriage	47(23.5%)	112(56%)	<0.001
Maternal anemia	89(44.5%)	95(47.5%)	0.312
Antepartum hemorrhage (APH)	13(6.5%)	47(23.5%)	<0.05
Postpartum hemorrhage (PPH)	5(2.5%)	11(5.5%)	0.12
Placental abruption	14(7.0%)	92(46.0%)	<0.001
Premature rupture of membranes (PROM)	11(5.5%)	56(28.0%)	<0.001
Preterm delivery	9(4.5%)	48(24%)	<0.05
Caesarean deliveries	35(17.5%)	78(39%)	<0.05

In Table 3, maternal adverse effects due to SCH are described. Gestational hypertension, miscarriage, antepartum hemorrhage, placental abruption, premature rupture of membranes (PROM), preterm delivery and Caesarean deliveries were significantly higher in pregnant women with SCH.

Table 4: Neonatal outcome associated with SCH.

Variables	Pregnancy with euthyroid(n=200)	Pregnancy with SCH(n=200)	P value
Low birth weight (LBW)	12	96	<0.001
Intrauterine growth restriction (IUGR)	10	21	<0.05
Low Apgar score (<7 5min after birth)	6	7	0.445
Stillbirth	2	3	0.235
Congenital anomaly	4	5	0.412
NICU admission	3	5	0.354

Different neonatal outcome of pregnancy with euthyroid state and with subclinical hypothyroidism are shown in Table 4.

Table 5: Anti TPO antibody titer in the study population.

Total n = 400	Anti TPO antibody titer <30IU/ml	Anti TPO antibody titer >30IU/ml	P value
Euthyroid (200)	167 (83.5%)	33 (16.5%)	P < 0.005
SCH (200)	52 (26%)	168 (84%)	P < 0.01

Discussion

Thyroid disorders are second most common endocrine disorders in women of reproductive age group [17]. The prevalence of subclinical hypothyroidism (SCH) in pregnancy is 37.69% [18]. On another study in Caucasian women the prevalence was 13.9%. In Iran, in a tertiary hospital, the prevalence of hypothyroidism was 4.9%, among those 89.1% were SCH patients. Ethnicity and environmental factors may also play a role. In a study in Egypt, targeted screening missed about 34.5% of pregnant women with thyroid disorders [19,20].

American Thyroid Association recommends screening of serum TSH at the age of 35 years and every 5years thereafter because of its high prevalence [21]. Women are at higher risk than men. In our study, mean age in pregnancy with euthyroid is 27.12 ± 0.05 and in pregnancy with SCH is 26.31 ± 0.25. Kalampoki et al. found the mean age 31.8 years and they revealed no association of parity with SCH. In this study also, no association with parity was found [22].

In this study mean TSH is 4.44 ± 0.11 mIU/L in 1st trimester, 4.74 ± 0.19 in 2nd trimester and 5.45 ± 0.17 in 3rd trimester. Ju et al. in 2016 also found raised TSH levels in three trimesters but normal serum T_4 level [27].

SCH may result into adverse pregnancy outcome as gestational diabetes mellitus (GDM), pregnancy induced hypertensive disorders, abruptio placentae etc. In several studies, GDM was highly associated with SCH [23].

Gestational hypertension and miscarriage are associated with SCH in this study. Casey et al. also found significantly higher cases of gestational hypertension, gestational diabetes mellitus (GDM) and miscarriage in pregnancy with SCH [24]. But in our study, no association between GDM and SCH is found. Nazarpour et al. in 2017 found significantly higher cases of abruptio placentae and pre-term delivery. But in APH, Caesarean deliveries and stillbirth there were no difference [25,26]. In our study, placental abruption, PROM, preterm delivery, APH and Caesarean deliveries are significantly higher in pregnancy with SCH. Ju et al. also found higher rate of PROM in SCH [27].

PPH and maternal anemia are not significantly higher in our study. But Zhao et al. in 2018 found significant correlation between PPH and maternal anemia with SCH in pregnancy [28]. Maraka et al. showed in their study that SCH not only affects maternal condition but also fetal outcome as intrauterine growth restriction (IUGR), small for gestational age (SGA), poor Apgar score in neonates [29]. In this study, low birth weight and IUGR babies were significantly higher in pregnant women with SCH.

Thyroid peroxidase (TPO) is an important enzyme, which is present in thyroid gland and regulates the production of thyroid hormone. Anti TPO antibody detects that the cause of thyroid disease is autoimmune. It may also rise in pregnancy, which detects the increased risk of future thyroid disorders. In this study, anti TPO antibody was significantly higher in pregnancy with SCH than pregnancy with euthyroid. Rao et al. in 2019 also found the similar result [30].

Conclusion

The cause of hypothyroidism was not determined in this study. Early diagnosis and management can cause effective prevention of adverse maternal and perinatal effects in pregnancy with subclinical hypothyroidism. Thyroid function tests should be included in every booking investigation of antenatal care. Further studies are recommended with larger sample.

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