International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Subclinical Hypothroidism and Its Impact on Pregnancy and Perinatal Outcome

Dr. Parmeshwor Junare[1], Dr. Laishram Trinity Meetei[2], Dr. Rajesh Singh Laishram[3], Dr. Lalrinchhani[4], Dr. N Nabakishore Singh[5], Dr. Lallan Prasad[6], Dr. Salam Ranabir[7]

[1]Ex- PGT, Department of Medicine, RIMS, Imphal, Manipur

[2]Assistant Professor, Department of Obstetrics and Gynaecology, RIMS, Imphal, Manipur

[3]Associate Professor, Department of Pathology, RIMS, Imphal, Manipur
Email: rajeshlaishr[at]gmail.com

[4]PGT, Department of Medicine, RIMS, Imphal, Manipur
Email: rinchhanufanai10[at]gmail.com

[5]Emeritus Professor, Department of Obstetrics and Gynaecology, RIMS, Imphal, Manipur

[6]Retired Professor, Department of Medicine, RIMS, Imphal, Manipur

[7]Associate Professor, Department of Medicine, RIMS, Imphal, Manipur

Corresponding Author:
Dr Salam Ranabir
Associate Professor, Department of Medicine, Regional Institute of Medical Sciences, Imphal, Manipur-795004
salamranabir[at]yahoo.co.in

Abstract: ***Background: Thyroid disorders including also subclinical hypothyroidism are commonly encountered during pregnancy and may have an effect on the fetal and maternal outcomes. The objectives of the present study were to study the perinatal outcomes and to look for maternal and fetal complication associated with subclinical hypothyroidism. Material and Methods: A case-control study was conducted in the Department of Medicine, in collaboration with department of Obstetrics and Gynaecology, at a tertiary care centre starting from October 2014 to September 2016. Pregnant women having subclinical hypothyroidism and pregnant women without subclinical hypothyroidism were the study population. Study variables included thyroid profile, examination of thyroid gland, abortion rate, period of gestation at delivery, mode of delivery, birth weight, Apgar score and condition of neonate at the time of birth. Women subclinical hypothyroidism were treated with levothyroxine (LT4).[2] The initial dose was depended on the women's serum Thyroid stimulating hormone (TSH) level. Their thyroid function was tested every 4 weeks and the drug dosage was adjusted according to their serum TSH level until delivery. The incidence of obstetrical and perinatal outcomes between women who received treatment was compared with normal women. Results: A total of 107 (one hundred seven) pregnant patients who (54 in SCH group and 53 in euthyroid group) were recruited. The distribution of age, gravida, and past obstetric history between the two groups which was comparable and not statistically significant. Majority of the diagnosis were made in the first and second trimester, which was statistically significant (p=0.035). Low birth weight was seen in 8 % of SCH group and 1.9 % of euthyroid group. Conclusion: The universal thyroid function testing during pregnancy and women with SCH should be offered treatment with levo thyroxine (LT4).***

Keywords: Subclinical hypothyroidism, Thyroid stimulating hormone, Thyroid profile, Apgar score

1. Introduction

Thyroid disorders are the second most common endocrinology disorders found in pregnancy. In pregnancy, overt hypothyroidism (OH) is seen in 4.58 % cases and subclinical hypothyroidism (SCH) in 6.47 % cases.[1] Recent studies from various parts of India have reported the prevalence of SCH during first trimester of pregnancy to range from 13.5 % to 34.4 %.[2, 3, 4, 5]

Untreated maternal hypothyroidism is associated with adverse fetal and obstetric outcomes. Fetal death rates are increased.[6] Early studies defined obstetric complication including miscarriages, anaemia in pregnancy, preeclampsia, abruption placenta and postpartum hemorrhage.[7] Premature birth, low birth weight (LBW), and increased neonatal respiratory distress have been described in babies born to hypothyroid mothers.[8] Complications are also reported in mothers with subclinical hypothyroidism. There is threefold risk of placental abruption and twofold risk of delivery before 34 weeks in mothers with subclinical hypothyroidism.[9] There is greater prevalence of subclinical hypothyroidism in women with delivery before 32 weeks compared to matched controls who delivered at term.[10] In retrospective study, it was noted that adequate treatment of overt and subclinical hypothyroidism minimized the risks of abortion and premature delivery regardless of initial thyroid status.[11]

Thyroid hormone deficiency may cause severe neurologic disorders resulting from deficit of neuronal cell differentiation and migration, axonal and dendritic out growth, myelin formation and synaptogenesis.[12] Low maternal thyroid hormone concentrations in early gestation

can be associated with significant decrements of intelligence quotient (IQ) of young children.[13]In population-based cohort of 3, 736 children whose maternal gestational thyroid function was correlated with subsequent childhood behaviour.[14]

There are few data/studies about the prevalence of thyroid dysfunction in pregnancy and perinatal outcome of subclinical hypothyroidism. Most of these studies are from western counterpart. It was, therefore, necessary to conduct the present study because findings of other studies may not apply to an Indian population. The objectives of the present study were to study the perinatal outcomes and to look for maternal and fetal complication associated with subclinical hypothyroidism.

2. Materials and methods

It was a case-control study conducted in the Department of Medicine, in collaboration with department of Obstetrics and Gynaecology, at a tertiary care centre for 2 (two) years, starting from October 2014 to September 2016. Pregnant women having subclinical hypothyroidism and pregnant women without subclinical hypothyroidism were the study population. Singleton pregnancy either primigravida or multigravida belonging to any age were included in the study. Multiple pregnancies or any other chronic medical illness (heart disease, liver disease, kidney disease) which might affect the course of pregnancy or interfere in the interpretation of thyroid function other than over thypothyroidism (OH) were excluded.

Written informed consent was obtained from all the study subjects, prior to the testing of thyroid hormones profile. The subjects underwent a detailed history taking, general physical examination, systemic examination and relevant laboratory investigations were done.

$$\frac{(1.96)^2\, p\,(100-p)}{e^2}$$

Sample size was calculated by the formula n= where ‘p’ was the positive character and ‘e’ was Standard error. The study was conducted on total 107 (one hundred seven) pregnant patients (54 in SCH group and 53 in euthyroid group) Study variables were thyroid profile, examination of thyroid gland, abortion rate, period of gestation at delivery, mode of delivery, birth weight, Apgar score and condition of neonate at the time of birth.

Serum levels of thyroid stimulating hormone (TSH), T4, and T3 were measured using SIEMENS ADVIA third generation chemilumin escence assay kit which has an intra-assay variability of <10 % for all the three parameters, inthe Department of Biochemistry. Women identified as having subclinical hypothyroidism according to American Thyroid Association guideline were treated with levothyroxine (LT4).[2] The initial dose was depended on the women’s serum TSH level. Their thyroid function was tested every 4 weeks and the drug dosage was adjusted according to their serum TSH level until delivery. The incidence of obstetrical and perinatal outcomes between women who received treatment was compared with normal women. The Statistical software SPSS 15.0 were used for the analysis of the data. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Students t test and Chi-square / Fisher Exact test were used to determine the significance of study parameter and p value <0.05 was considered significant.

3. Results

The study includes total 107 pregnant women, 54 in SCH group and 53 in euthyroid group. SCH women were treated with levothyroxine (LT4). Table I shows the distribution of age, gravida, and past obstetric history between the two groups which was comparable and not statistically significant. No significant difference was seen between the mean age and in respect to abortion and caesarean section. This is particularly important to highlight the importance of current at-risk pregnancy and past LSCS also affect the mode of delivery in current pregnancy

Majority of the diagnosis were made in the first and second trimester, which was statistically significant (p=0.035). However, the mean time of diagnosis was comparable 13.94 ±7.06 weeks and 14.05 ±5.99 weeks in euthyroid group and SCH group respectively as shown in table II. The mean TSH in euthyroid group was 1.61±0.63 mIU/ml and 5.84 ±3.06 mIU/ml in SCH group, which was statistically significant (p<0.001) as shown in table II. The complications noted in both the groups are shown in table III, which was comparable and not statistically significant.

Preterm delivery was noted in 3 (6 %) patients in SCH group and none in euthyroid group. However, the mean period of gestation at delivery was 38.38±1.49 in SCH group and 38.62±2.23 weeks in euthyroid group as shown in table IV. This was of nostatistical significance (p=0.130). Table IV also shows caesarean section and vaginal delivery rate of 61.5 % and 38.5 % in euthyroid and 62 % and 38 % in SCH group respectively and this was not statistically significant (p=0.288). Low birth weight was seen in 8 % of SCH group and 1.9 % of euthyroid group as shown in table V.

4. Discussion

Thyroid disorder is the one of several risk factors for spontaneous abortion. The incidence of spontaneous abortion in women with high TSH level was higher than in women with normal TSH level in our study, which agreed with other studies. In a study by Allan et al, [6]the rate of fetal death in women with TSH≥6 mIU/l was significantly higher than in women with TSH<6 mIU/l. Abalovich et al[11] reported the abortion rate of 71.4 % in SCH when treatment with LT4 was inadequate. This is consistent with the findings of our study, with LT4 treatment there is decreased incidence of spontaneous abortions (7.4 %) in women with SCH compared to previous studies where no treatment or inadequate treatment was given in SCH pregnant women.

The incidence of gestational hypertension (GHTN) and pre-eclampsia was significantly higher in the OH and SCH

patients than in the general population in previous study.[8] Leung AS et al[8] found 11 % incidence of GHTN and 6 % for pre-eclampsia in SCH pregnant women. In our study, one case of gestational hypertension (1.9 %) and another case of pre-eclampsia seen in SCH women. This lower rate may be due to effect of LT4 treatment as it is well known fact that thyroid dysfunction is the cause of reversible hypertension. Another possible reason for this is relatively small number of SCH women in our study.

Pregnant women with SCH were 3 times more likely to experience placental abruption in SCH group 4/404 (1 %) vs. 52/15, 689 (0.3 %) in euthyroid group as reported by Casey et al[10], while another study by Wang et al[15] showed no significant association between SCH and placental abruption. In our study, there is no case of placental abruption in SCH group; this may be due to effect of LT4 treatment as thyroid hormone is required 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.[15, 16] This different finding may be due small sample size of our study and different genetic makeup of our population.

Mean period of gestation in our study is 38.38±1.49 weeks in SCH group and 38.62±2.23 weeks in euthyroid group. This agrees with the previous study by Casey et al.[10] Preterm delivery rate of 10.3 % was observed in one study from India.[1] In study by Abalovich et al,[11] term delivery rate of 21.4 % and 90.5 % was seen when treatment was inadequate and adequate respectively in SCH.[11] In our study, preterm delivery rate is 3/50 (6 %), which is less compared to previous studies. There is decreased rate of preterm delivery with treatment and this finding in our study is consistent with the findings of other studies.[11]

Previous studies had shown the increased rate of Caesarean section in women with SCH as compared to euthyroid women.[1, 10] In our study, LSCS rate is similar 31/50 (62 %) in SCH group vs. 32/52 (61.5 %) in euthyroid group. LSCS rate is high in both the groups, the reason being the tertiary care teaching hospital where referral cases are sent. Also, in our study indication for LSCS was mostly due to previous LSCS and other common obstetrical indications, which is standard practice in obstetrics. Only in one case, fetal bradycardia was the indication for LSCS in SCH group. We cannot comment whether SCH is associated with higher LSCS rate, as there was only a single case of fetal distress as an indication for LSCS in SCH group in our study and in other cases common obstetrical indications were the reason for LSCS.

Complications of delivery like post-partum hemorrhage is seen in a single case in both the groups (1.9 %) in our study. The mean birth weight was 2.96±0.40 kg in SCH group vs. 3.10±0.48 kg in euthyroid group which is comparable in both the groups (P=0.286). The slight low weight in SCH group may be due effect of SCH or it may be due difference in demographic and biologic characteristics of normal women. Casey et al[10] found the LBW rate of 6 % in 404 non treated SCH women vs. 5 % in 15, 689 normal women studied, while other study had shown LBW rate of 2.38 % in non-treated SCH group vs.2.77 % in 542 normal women.[15] We find the rate of low birth weight (LBW) of 4/50 (8 %) in SCH group and 1/52 (1.9 %) normal group. The reason for low rate of LBW in normal group, may be the small number of normal women (n=53) in our study compared to previous studies.

Sahu et al[1] noted the Apgar score of below 7 at 5 minutes in 12.9 % in SCH group vs. 5.3 % in normal group when no treatment was given to SCH women. In our study there is no case of Apgar score below 7, possible reason behind this may be due effect of treatment in SCH group or it could be due to high rate of LSCS in both the groups as elective LSCS may have beneficial effect on possible fetal distress.

In our study neonatal hospitalization rate in SCH group is 2/50 (4 %). Out of two neonates hospitalized 1 neonate was hospitalized because of respiratory distress while other had femur fracture. There is no statistically significant difference in hospitalization rate in two groups. Previous study by Sahuet al[1] had noted high-rate neonatal complication (12.9 %) in SCH women. Our study shows improvement in neonatal hospitalization rate with treatment of SCH.

Carty et al,[17] reported that women with TSH>5 mU/L delivered infants with lower birth weight than women with TSH<2.5mU/L. However, there was no difference in other obstetric outcomes. Barisic et al,[18] reported the highest incidence of SCH in women with preeclampsia compared to those pregnant women with hypertension, GDM and uncomplicated pregnancies (controls). TSH levels were higher in those with preeclampsia and hypertension compared to controls. However, there was no difference in TSH level between women with GDM and controls. In Japanese women without known medical complications pregnant women with TSH between 3.0-10.0 mIU/L had higher incidence of GDM. But there was no significant difference in other maternal and neonatal outcome compared to euthyroid women with negative anti thyroid peroxidise antibody (Anti TPOAb).[19]

In a study from United States, SCH pregnant women (TSH: 2.5-10 mIU/L) who received treatment had significantly lesser pregnancy loss than those untreated.[20] After adjustment for potential confounders such as age, TSH level, ethnicity, income, Charlson index, hypertension, obesity, history of thyroid disease, and history of pregnancy loss, those who received treatment had 38 % lower odds of pregnancy loss compared to those untreated. However, treated women had higher adjusted odds of preterm delivery and preeclampsia compared to untreated women. The benefit of treatment on pregnancy loss was observed only among women with pre-treatment TSH of 4.1-10.0 mIU/L but not in those with TSH of 2.5-4.0 mIU/L.[20] In another study, 26.9 % had TSH>2.5 mIU/L and women with TSH 2.5-5.0 mIU/L had higher risk of perinatal loss and miscarriage.[21] There was trend towards prematurity but there was no association with preeclampsia, dystocia of labour and stillbirths. After adjustment for mother's age the effect persisted for perinatal loss, miscarriage, and premature birth. Those with TSH>5.0 mIU/L treated to a target of 2.5 mIU/L showed no difference in the risk of having adverse outcomes compared to those with TSH≤2.5 mIU/L at first trimester.[21]

Some other study could not demonstrate any association of maternal, fetal and neonatal adverse outcome with the exception of preterm delivery before 34 weeks with SCH which is dose dependent to TSH level.[22] In a meta-analysis, there is a significant association between maternal SCH in pregnancy and child intellectual development and child motor development. Significant effect of maternal SCH in pregnancy on birth weight (BW) was also seen. Maternal SCH was a risk factor for LBW.[23] In another study by Nasikandy,[24] the incidence of preterm birth was higher among women with SCH compared to euthyroid women. There was no evidence of an effect of maternal SCH on the risk of intellectual impairment in children in studies with TSH measurement before 12 weeks.[25]

In a study of singleton pregnancy before 20 weeks of gestation, women with SCH (TSH≥4.0mIU/L) or hypothyroxinemia were randomly assigned to LT4 therapy or placebo. There was no significant difference in neurocognitive outcomes of the children at 5 years of age or pregnancy outcomes between those on LT4 and placebo.[26] Nazarpour et al, [27] reported no difference in preterm delivery and neonatal admission among TPOAb positive women with TSH<4mIU/L with or without LT4 treatment. However, there was significant difference among women those with TSH≥4mIU/L. Among TPOAb negative with TSH of 2.5-4.0mIU/L there was no significant difference in preterm delivery between those treated with LT4 and those without. But when TSH cut-off of 4.0 mIU/L was adopted, there was significant difference in preterm delivery between those on LT4 and without.[28]

SCH women who received LT4 in 8-10weeks gestation had lower rate of pregnancy complications and adverse outcomes compared to women who received LT4 in second trimester or untreated. Among TPOAb positive women, treatment at second trimester had lower complication compared to those untreated.[29] Another study found that second trimester LT4 therapy for SCH or hypothyroxinemia does not improve cognitive outcomes of children. However, no difference was noted in preterm births, gestational hypertension, GDM, neonatal death, Apgar score or other adverse effects.[30]

Among women with SCH (TSH value of 2.5-10mIU/L) who were treated with LT4 in first trimester (7-11 weeks), there was no difference in complications of pregnancy like pregnancy induced hypertension (PIH), antepartum haemorrhage (APH), abruption of placenta, premature labour, and premature rupture of membranes (PROM) compared to euthyroid women. However, SGA occurred in higher number of treated SCH women which was close to significance (p=0.050).[31] In another study with LT4 treatment for SCH, the incidence of PROM, gestational diabetes mellitus (GDM), fetalmacrosomia and post-partum haemorrhage (PPH) decreased significantly in the women who achieved TSH target by 4 weeks compared to those who reached target in 4-8 weeks and >8 weeks. Untreated women had significantly higher risk for GDM and fetalmacrosomia.[32]

Among SCH women who were treated with LT4 to maintain TSH between 0.3-3 mIU/L irrespective of TPOAb status there no difference in incidence of PIH, APH or PPH, preterm delivery, and spontaneous abortion.[33] Women with history of recurrent abortion had a higher prevalence of TPOAb positivity compared to healthy pregnant women. With treatment with LT4 there was no difference in prevalence of miscarriage between TPOAb positive SCH and euthyroid women.[34] In the meta-analysis by Zhang et al. prevalence of miscarriage was much higher among women with SCH compared to euthyroid. Miscarriage rate is increased among women with thyroid autoimmunity. But there was no difference in miscarriage in SCH women who received LT4 compared to euthyroid.[35]

TPOAb and free T4 estimation were not carried out in all pregnant women, for cost effectiveness in low resource setting. There are possibilities that this strategy would have missed the patient with isolated hypothyroxinemia (low FT4 and normal TSH) and women who are antibody positive.

Women with serum TSH between 3.1-6.2 mIU/L had similar maternal and fetal outcomes compared to women with TSH between 0.4-3.0. There was no difference in the mode of delivery between the groups.[36]There is increased rates in miscarriages, LBWs, preterm deliveries <34 weeks in anti-TPO Ab positive euthyroid women compared to euthyroid TPOAb negative women.[37] Anti-TPO positive, euthyroid females had a higher prevalence of infertility, anaemia and preterm delivery as compared to the controls.[38]

Miscarriages and preterm deliveries were significantly increased among TPOAb positive euthyroid women compared to euthyroid TPOAb negatives. Other pregnancy related complications like intrauterine fetaldeath (IUD), intrauterine growth restriction (IUGR), preeclampsia and PIH were not different.[39] Increased incidence of miscarriage was observed in anti-TPO positive mothers when compared to antibody negative mothers.[40]

A meta-analysis conducted by Zhang Y et al,[35] also shows that compared with isolated subclinical hypothyroidism, the prevalence of miscarriage risk in patients with thyroid autoimmunity is significantly increased. Anothermeta-analysis by Prummel et al[41] shows that TPO Ab was associated with two-fold greater risk of miscarriage. Some other study had reported 2-3 folds increase in preterm delivery in euthyroid/subclinical TPO Ab pregnant women whereas others did not report this association.[42]

The weakness of our analysis is small sample size of euthyroid women compare to all previous studies. Cord TSH measurement was not done in our study to look for neonate with congenital hypothyroidism or possible under or overtreatment.

5. Conclusion

To conclude, considering the possible adverse obstetrical and perinatal effects of SCH during pregnancy, we suggest the universal thyroid function testing during pregnancy. Trimester specific TSH ranges should be use while interpreting thyroid profile during pregnancy. Women with SCH should be offered treatment with LT4.

References

[1] Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. Arch of Gynecol and Obstet. 2010; 281 (2): 215-20.
[2] Dhanwal DK, Prasad S, Agarwal AK, Dixit V, Banerjee AK. High prevalence of subclinical hypothyroidism during first trimester of pregnancy in North India. Indian J EndocrInol Metab. 2013; 17: 281-4.
[3] Jebasingh FK, Salam R, Meetei TL, Singh NN, Prasad L. Thyroid status of the pregnant women of Manipur: A comparison of American Thyroid Association guidelines and normal laboratory reference range. Thyroid Res Pract. 2015; 12: 67-70.
[4] Mandal RC, Bhar D, Das A, Basunia SR, Kundu SB, Mahapatra C. Subclinical hypothyroidism in pregnancy: An emerging problem in Southern West Bengal: A cross-sectional study. J Nat Sc Biol Med. 2016; 7: 80-4.
[5] Rajput R, Goel V, Nanda S, Rajput M, Seth S. Prevalence of thyroid dysfunction among women during the first trimester of pregnancy at a tertiary care hospital in Haryana. Indian J Endocrinol Metab. 2015; 19 (3): 416-9.
[6] Allan WC, Haddow JE, Palomaki GE, Williams JR, Mitchell ML, Hermos RJ, et al,. Maternal thyroid deficiency and pregnancy complications: implications for population screening. J Med Screen. 2000; 7 (3): 127-30.
[7] Davis LE, Leveno KJ, Cunningham FG. Hypothyroidism complicating pregnancy. Obstet Gynecol. 1988; 72 (1): 108-12.
[8] Leung AS, Millar LK, Koonings PP, Montoro M, Mestman JH. Perinatal outcome in hypothyroid pregnancies. ObstetGynecol 1993; 81 (3): 349-53.
[9] Idris I, Srinivasan R, Simm A, Page RC. Maternal hypothyroidism in early and late gestation: effects on neonatal and obstetric outcome. Clin Endocrinol. 2005; 63 (5): 560-5.
[10] Casey BM, Dashe JS, Wells CE, Mclntire DD, Byrd W, Lenovo KJ, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstet Gynecol. 2005; 105: 239-45.
[11] Abalovich M, Gutierrez S, Alcaraz G, Maccallini G, Garcia A, Levalle O. Overt and subclinical hypothyroidism complicating pregnancy. Thyroid.2002; 12 (1): 63-8.
[12] Bernal J. Thyroid hormone receptors in brain development and function. Nat Clin Pract Endocrinol Metab.2007; 3 (3): 249-59.
[13] Li Y, Shan Z, Teng W, Yu X, Fan C, Tenq X, et al. Abnormalities of maternal thyroid function during pregnancy affect neuropsychological development of their children at 25-30 months. Clin Endocrinol.2010; 72 (6): 825-9.
[14] Ghassabian A, Bongers-Schokking JJ, Henrichs J, Jaddoe VW, Visser TJ, Visser W, et al,. Maternal thyroid function during pregnancy and behavioral problem in the offspring: the generation R study. Pediatr Res.2011; 69 (5): 454-9.
[15] Wang S, Teng WP, Li JX, Wang WW, Shang ZY. Effects of maternal subclinical hypothyroidism on obstetrical outcomes during early pregnancy. J Endocrinol Invest 2012; 35 (3): 322-5.
[16] Walker JJ. Pre-eclampsia. Lancet.2000; 356: 1260-5.
[17] Carty DM, Doogan F, Welsh P, Dominiczak AF, Delles C. Thyroid stimulating hormone (TSH) ≥2.5mU/L in early pregnancy: Prevalence and subsequent outcomes. Eur J ObstetGynaecolReprod Biol.2017; 210: 366-9.
[18] Barisic T, Mandic V, Vasilj A, Tiric D. Higher levels of thyrotropin in pregnancy and adverse pregnancy outcomes. J MaternFetal Neonatal Med.2019; 32: 2883-2888.
[19] Furukawa S, Miyakawa K, Shibata J, Iwashita M. Women with subclinical hypothyroidism are at low risk of poor pregnancy outcome in Japan. Tohoku J Exp Med., 2017; 242 (3): 167-72
[20] Maraka S, Mwangi R, McCoy RG, Yao X, Sangaralingham LR, Ospina NMS, et al. Thyroid hormone treatment among pregnant women with subclinical hypothyroidism: US national assessment. BMJ.2017; 356: i6865.
[21] Hernandez M, Lopez C, Soldevilla B, Cecenarro L, Martinez-Barahona M, Palomera E, et al,. Impact of TSH during the first trimester of pregnancy on obstetric and fetal complications: Usefulness of 2.5 mIU/L cut-off value. Clin Endocrinol.2018; 88 (5): 728-734.
[22] Arbib N, Hadar E, Sneh-Arbib O, Chen R, Wiznitzer A, Gabbay-Benziv R. First trimester thyroid stimulating hormone as an independent risk factor for adverse pregnancy outcome. J MaternFetal Neonatal Med.2017; 30 (18): 2174-2178.
[23] Lui Y, Chen h, Jing C, Li F. The association between maternal subclinical hypothyroid and growth, development and childhood intelligence. A meta analysis. J Clin Res Pediatr Endocrinol.2018; 10 (2): 153-161.
[24] Nasirkandy MP, Badfar G, Shohani M, Rahmati S, YektaKooshali MH, Abbasalizadeh S, et al,. The relationship of maternal hypothyroidism and hypothyroxinemia during pregnancy on pre-term birth: An updated systemic review and meta-analysis. Int J Reprod BioMed 2017; 15 (9): 543-552.
[25] Thompson W, Russell G, Baragwanath G, Matthews J, Vaidya B, Thompson-Coon J. Maternal thyroid hormone insufficiency during pregnancy and risk of neurodevelopmental disorders in offspring: A systemic review and meta-analysis. Clinical Endocrinol.2018; 88: 575-584.
[26] Casey BM, Thom EA, Peaceman AM, Varner MW, Sorokin Y, Hirtz DG, et al. Treatment of Subclinical Hypothyroidism or Hypothyroxinemia in Pregnancy. N Engl J Med.2017; 376 (9): 815-25.
[27] Nazarpour S, Tehrani FR, Simbar M, Tohidi M, Majd HA, Azizi F. Effects of levothyroxine treatment on pregnancy outcomes in pregnant women with autoimmune thyroid disease. Eur J Endocrinol.2017; 176: 253-65
[28] Nazarpour S, Tehrani FR, Simbar M, Tohidi M, Minooee S, Rahmati M, et al,. Effects of levothyroxine on pregnant women with subclinical hypothyroidism,

negative for thyroid peroxidase antibodies. J Clin Endocrinol Metab.2018; 103 (3): 926-35

[29] Zhao L, Jiang G, Tian X, Zhang X, Zhu T, Chen B, et al. Initiation timing effect of levothyroxine treatment on subclinical hypothyroidism in pregnancy. Gynecol Endocrinol.2018; 34 (10): 845-848.

[30] Stagnaro-Green A. Second trimester levothyroxine treatment for subclinical hypothyroidism or hypothyroxinemia of pregnancy does not improve cognitive outcomes of children. Evid Based Med.2017.10.1136/ebmed-2017-110743.

[31] Blumenthal NJ, Eastman CJ. Beneficial Effects on Pregnancy Outcomes of Thyroid Hormone Replacement for Subclinical Hypothyroid. J Thyroid Res 2017; 2017: 4601365.

[32] Ju R, Lin Y, Long Y, Zhang J, Huang J. Clinical efficacy of therapeutic intervention for subclinical hypothyroidism during pregnancy. Genet Mol Res.2016; 15 (4): gmr15049019.

[33] Jayaraman M, Verma A, Harikumar KVS, Ugale M, Modi K. Pregnancy outcomes with thyroxine replacement for subclinical hypothyroidism: Role of thyroid autoimmunity. Indian J Endocrinol Metab.2013; 17: 294-7.

[34] Lata K, Dutta P, Sridhar S, Rohilla M, Srinivasan A, Prashad GRV, Shah VN, Bhansali A. Thyroid autoimmunity and obstetric outcomes in women with recurrent miscarriage: A case-control study. Endocr Connect.2013; 2 (2): 118-24.

[35] Zhang Y, Wang H, Pan X, Teng W, Shan Z. Patients with subclinical hypothyroidism before 20 weeks of pregnancy have a higher risk of miscarriage: A systemic review and meta-analysis. PLoS One.2017; 12 (4): e0175708.

[36] Joshi D, Dewan R, Bharti R, Thariani K, Sablok A, Sharma M, et al,. Feto-maternal outcome using new screening criteria of serum TSH for diagnosing hypothyroidism in pregnancy. J Clin Diagn Res.2015; 9 (4): QC01-3.

[37] Aruna M, Nagar P. Pregnancy outcome in euthyroid women with anti-Thyroid peroxidase antibodies. J ObstetGynaecol India.2016; 66 (3): 160-5.

[38] Meena M, Chopra S, Jain V, Aggarwal N. The Effect of Anti-Thyroid Peroxidase Antibodies on Pregnancy Outcomes in Euthyroid Women. J Clin Diagn Res.2016; 10 (9): QC04-QC07.

[39] Rajput R, Yadav T, Seth S, Nanda S. Prevalence of thyroid peroxidase antibody and pregnancy outcome in euthyroid autoimmune positive pregnant women from a tertiary care center in Haryana. Indian J Endocrinol Metab.2017; 21: 577-80.

[40] Bhattacharyya R, Mukherjee K, Das A, Biswas MR, Basunia SR, Mukherjee A. Anti-thyroid peroxidase antibody positivity during early pregnancy is associated with pregnancy complications and maternal morbidity in later life. J Nat Sci Biol Med.2015; 6 (2): 402-5.

[41] Prummel MF, Weirsinga WM. Thyroid autoimmunity and miscarriage. Eur J Endocrinol.2004; 150: 751-5.

[42] Teirney K, Delpachitra P, Grossmann M, Onwude J, Sikaris K, Wallace EM, et al,. Thyroid function and autoatibody status among women who spontaneously deliver under 35 weeks of gestation. Clin Endocrinol.2009; 71: 892-5.

Tables

Table I: Table showing the distribution of age, gravida, and obstetric history

Variables	Euthyroid group	SCH group	Total
Age < 20 years	1 (1.9 %)	2 (3.7 %)	3 (2.8 %)
Age 20-30 years	25 (47.2 %)	26 (48.1 %)	51 (47.7 %)
Age 30-40 years	27 (50.9 %)	26 (48.1 %)	53 (49.5 %)
Mean ± SD	30.66 ± 5.42	29.35 ± 6.45	30.00±5.97
G1	17 (32.1 %)	19 (35.2 %)	36 (33.6 %)
G2	16 (30.2 %)	22 (40.7 %)	38 (35.5 %)
G3	12 (22.6 %)	7 (13 %)	19 (17.8 %)
G4	5 (9.4 %)	4 (7.4 %)	9 (8.4 %)
G5	1 (1.9 %)	1 (1.9 %)	2 (1.9 %)
G6	2 (3.8 %)	1 (1.9 %)	3 (2.8 %)
Abortion	14 (26.4 %)	14 (25.9 %)	28 (26.2 %)
LSCS*	12 (22.6 %)	8 (14.8 %)	30 (28 %)
H/O IUFD*	1 (1.9 %)	0	1 (0.9 %)
H/O Down syndrome	1 (1.9 %)	0	1 (0.9 %)

*LSCS = lower segment caesarean section, IUFD = intrauterine fetal death, H/O = history of

Table II: Time of diagnosis according to trimester and TSH level

Time of diagnosis	Euthyroid	SCH
First	24 (45.3 %)	34 (63 %)
Second	27 (50.9 %)	14 (25.9 %)
Third	2 (3.8 %)	6 (11.1 %)
Mean ± SD	13.98±7.06	14.05 ±5.99
p=0.035*, significant, Chi-Square test		
TSH level		
<2.5	50 (94.3 %)	0 (0 %)
2.5-3	3 (5.7 %)	2 (3.7 %)
>3	0 (0 %)	52 (96.3 %)
Mean ± SD	1.61±0.63	5.84±3.06
p<0.001**, significant, student t test		

Table III: Table showing the complication detected in both the groups

Variables	Euthyroid	SCH	Total	P value
Abortion	1 (1.9 %)	4 (7.4 %)	5 (4.7 %)	0.363
Placenta previa	0	1 (1.8 %)	1 (0.9 %)	1.000
Abruptio	1 (1.9 %)	0	1 (0.9 %)	0.495
Gestational Hypertension	0	1 (1.9 %)	1 (0.9 %)	1.000
Pre-eclampsia	1 (1.9 %)	1 (1.9 %)	2 (1.9 %)	1.000
PROM*	0	3 (5.5 %)	3 (2.8 %)	0.243
PPH	1 (1.9 %)	1 (1.9 %)	2 (1.9 %)	1.000

*PROM= Premature rupture of membranes PPH=post partum haemorrhage

Table IV: Table showing period of gestation and mode of delivery

Period of Gestation at delivery (weeks)	Euthyroid	SCH	Total
28-32	0 (0 %)	0 (0 %)	0 (0 %)
32-37	0 (0 %)	3 (6 %) /	3 (2.9 %)
37-40	42 (80.8 %)	42 (84 %)	84 (82.4 %)
40-42	10 (19.2 %)	5 (10 %)	15 (14.7 %)
Mean ± SD	38.62±2.23	38.38±1.49	38.51±1.91
	52 (100 %)	50 (100 %)	102 (100

			%)
p = 0.130, Not significant, Student t test			
Mode of Delivery			
Lower Segment Caesarean Section (LSCS)	32 (61.5 %)	31 (62 %)	63 (61.8 %)
Normal Vaginal Delivery (NVD)	16 (30.8 %)	19 (38 %)	35 (34.3 %)
Ventouse	3 (5.8 %)	0 (0 %)	3 (2.9 %)
Vaginal birth after caesarean (VBAC)	1 (1.9 %)	0 (0 %)	1 (1 %)
Total	52 (100 %)	50 (100 %)	102 (100 %)
p = 0.288, Not significant, Fisher Exact test			

Table V: Birth Weight (kg) and Apgar score (AS)

Variables	Euthyroid	SCH	Total
<2.5 kg	1 (1.9 %)	4 (8 %)	5 (4.9 %)
2.5-3.5 kg	43 (82.7 %)	41 (82 %)	84 (82.4 %)
>3.5 kg	8 (15.4 %)	5 (10 %)	13 (12.7 %)
Mean ± SD	3.10±0.48	2.96±0.40	3.03±0.44
p =0.286, Not significant, Fisher Exact test			
AS < 7	0	0	0 (0 %)
AS > 7	52	50	102 (100 %)
p =1.000, Not significant, Fisher Exact test			